MONTHLY VARIATION IN INFANT WEIGHT AND LENGTH GROWTH IN RURAL UTTAR PRADESH, INDIA

A Dissertation

Presented to the Faculty of the Graduate School

of Cornell University

In Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy

by

Emily Marcene Madan

May, 2018

MONTHLY VARIATION IN INFANT WEIGHT AND LENGTH GROWTH IN RURAL UTTAR PRADESH, INDIA

Emily Marcene Madan, Ph.D.

Cornell University 2018

India has the highest number of undernourished children in the world. Rural agriculturalists suffer a high burden of undernutrition and are exposed to health and nutrition risks that vary throughout the year. Recent estimates of undernutrition based on growth from 0-6 months of age are high, but the risk factors for this poor growth are understudied.

Pregnant women (n=599) were recruited from nine selected villages in Shivgarh, Uttar Pradesh for a longitudinal study. Mother-infant pairs were visited monthly from 0-6 months of infant age. Repeated maternal and infant health information and anthropometry were collected.

Gestational age and maternal height were associated with larger newborn size. Female sex, primiparity, and being food insecure were associated with smaller newborn size. Compared to the overall sample means, infants conceived from July-September 2014 and April-June 2014 were approximately 200 g lighter (p=0.02) and 0.5 cm shorter (p=0.08), respectively. Infants who began the 1-4 month interval of growth from August-October 2015 had rates of length growth that were 0.064 ± 0.016 cm/month lower (p<0.001). We observed no monthly differences in rates of weight growth. In the 1-4 month growth interval, female sex and maternal work in agriculture were associated with slower rates of growth. Exclusive breastfeeding was associated with faster rates of growth. Newborn length and maternal morbidity were associated with slower and faster rates of length growth, respectively. Primiparity and newborn weight were associated with faster rates of weight growth ($p<0.1$). Unvaccinated infants had significantly slower growth related to increased morbidity (interaction $p=0.001$). Infants born from August-October 2015 had significantly slower length growth related to increased time spent in childcare (interaction $p=0.019$).

This research shows that both prenatal and early postnatal determinants of poor growth contribute to small size at six months of age and confirms the important predictors of growth observed in other settings. Season was a relatively weak predictor of growth in this setting, but may be a stronger predictor in primarily rain-fed agricultural areas. Intervention strategies to address modifiable risk factors for poor infant growth are needed during both the prenatal and postnatal periods for positive impacts on early postnatal growth.

BIOGRAPHICAL SKETCH

Emily Marcene Madan was born and raised in Vestal, New York. In 2007, she graduated from Cornell University with a Bachelors of Science in Nutrition with Distinction in Research. She then spent 2008 conducting research with the Polish Academy of Sciences on a Fulbright scholarship before entering the graduate program in International Nutrition at Cornell University in 2009.

ACKNOWLEDGMENTS

I would like to thank my advisor, Dr. Jere Haas, for his generous engagement in this research in both Ithaca and India. I am grateful for the mentorship and knowledge he has provided to me as both an undergraduate and a graduate student. I am especially grateful that I had the chance to learn from him in the field, where his creativity really shines. I would also like to thank the members of my committee. Dr. Kathleen Rasmussen provided an incredible amount of support and encouragement at some of the most difficult times during this dissertation. She has challenged me to grow both personally and intellectually. Dr. Edward Frongillo provided invaluable support for the methodologies used in this research. This dissertation would not have been possible without him. I am especially grateful for his mentorship in South Carolina and for his time during all the Skype calls along the way. Dr. Purnima Menon championed this research, and the project would not have happened without her. I am grateful to her for opening her home to me, and for providing mentorship and support during my time in India. I would like to thank Drs. David Pelletier and Christopher Barrett for the wonderful insights that they brought to this research during my committee meetings and exams over the years. They have challenged me to examine problems in new ways and it is because of them that I received so much benefit from my minor fields. A special thank you to Dr. Bradley Rickard for acting as a proxy for my defense.

Thank you to Dr. Vishwajeet and Mrs. Aarti Kumar for their collaboration on this research. The project would not have been possible without them and their wonderful team at the Community Empowerment Lab. Thank you especially to Ms. Shambhavi Singh, Dr. Swati Dixit, Mr. Amit Tandon, Mr. Sharad Yadav, and Mr. Amit Verma who were the backbone of the data collection and management of the research. I am extremely grateful to our dedicated team of enumerators who made the data collection a reality, and to all the mothers and families of Shivgarh for inviting us into their community and homes.

This research was possible because of the generous funding from Agriculture for Health and Nutrition (A4HN) and Leveraging Agriculture for Health and Nutrition in South Asia (LANSA). I would like to thank Dr. Stuart Gillespie in particular for his support and mentorship. Thank you also to the Division of Nutritional Sciences (DNS) and the South Asia Foreign Language and Area Studies program for their financial support.

During this dissertation, I received excellent guidance on data cleaning and management, and analyses from the Cornell Statistical Consulting Unit, and I would like to thank Francoise Vermeylen and Erika Mudrak, in particular for their support. I have learned a great deal from both of them. I would also like to thank Michael Ko and Marika Cusick for the hard work to help clean and organize the data for this dissertation. I am also incredibly grateful to my colleagues and friends from DNS and the International Food Research Policy Institute Delhi Office, who have been amazing sources of intellectual and emotional support.

I would like to thank my parents, Emil and Bonnie, my brother, Adam, and my sister, Melissa, for their support through the victories and defeats of this process. A lot of Bielecki family sarcasm, medical diagnoses, board games, and drinking fueled this journey. Lastly, to my husband, Sanchay, thank you for moving around the world for this dissertation with me, and for always making arrangements for my emotional support dogs, Lola and Delilah, to be there too. Thank you for encouraging me to finish, but reminding me that I did not have to.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

AGA: Appropriate for gestational age
AHMANI: Community Empowerment Lab pregnancy surveillance project
ANOVA: Analysis of variance
BMI: Body mass index
CEL: Community Empowerment Lab
cm: centimeters
DDS: Diet diversity score
ENS: early neonatal size
FANTA: Food and Nutrition Technical Assistance
g:grams
Gest age: gestational age
HAZ/LAZ: Height-for-age Z-score/ Length-for-age Z-score
HFIAS: Household Food Insecurity Access Scale
IUGR: Intrauterine growth restriction
IFPRI: International Food Policy Research Institute
IGF-1: Insulin-like growth factor 1
kg: Kilograms
LBW: Low birth weight
MAR: Missing at random
MGRS: Multicentre Growth Reference Study
MNS: Maternal nutritional status
mo: months
NCHS/WHO: National Center for Health Statistics/World Health Organization
NFHS: National Family Health Services
NGO: non-governmental organization
PCA: Principal components analysis
PA: Physical activity
PI: ponderal index
SD: Standard deviation
SES: Socio-economic status
SGA: Small-for-gestational age
TEM: Technical error of measurement
UNICEF: United Nations Children's Fund
WAZ: Weight-for-age Z-scores
WHO: World Health Organization
WHZ/WLZ: Weight-for-height Z-score/ Weight-for-length Z-score
y: years

CHAPTER 1
Introduction

1.1 Child undernutrition: A global public health problem

Various measures of nutritional status are widely used to define undernutrition and include assessments of dietary intake, clinical signs of deficiency and biochemical indicators. However, anthropometric assessment of body size and body composition remains one of the most widely used and accepted methods of assessment, particularly in children from low-resource settings [1]. The definition of undernutrition is based on a negative deviation in child growth, or growth faltering, relative to an age appropriate reference or standard and can be described as stunting (low length or height-for-age), wasting (low weight-for-length or height), or underweight (low weight-for-age). Child undernutrition remains a significant global public health challenge. Around the world, 165 million children less than five years of age (26%) are stunted and about 17% of child deaths are attributed to undernutrition (stunting) [2]. Although some progress has been made in reducing undernutrition in recent years, the progress has been unequal across regions. South-Central Asia has the highest number of undernourished children in the world (69 million), and India alone contributes the majority of this burden [2]. Risk factors associated with undernutrition vary somewhat depending on the manifestation and severity of the condition, but, in general, children who are undernourished are at life-long increased risk of morbidity and mortality, cognitive deficits, and decreased adult productivity and earnings [2, 3]. It is also widely accepted that the first "1000 days" (the period from conception to approximately two years of age) are a critical period for addressing deficits in child growth. After two years of age, deficits, particularly in height, are considered a largely irreversible phenomenon [3-5]. Therefore, understanding and addressing undernutrition in early life is of critical public health importance.

1.2 Undernutrition in India

Despite some reduction in recent years, child undernutrition in India is widespread. For 2015-2016, nationwide rates of stunting, wasting and underweight in children less than five years of age were 38.4%, 21% and 35.7%, respectively [6]. Since 2005, the prevalences of stunting and underweight have decreased, but the prevalence of wasting has increased [7]. Other health and nutrition indicators suggest a similarly dire situation. Among women of reproductive age, macro-and micronutrient deficiencies are rampant (33% low body mass index (BMI); 56% anemia) [7]. Infant mortality is 41 per 1,000 live births and only about 55% of children less than six months of age are exclusively breastfed [6].

1.3 Changing assessment of undernutrition: the NCHS/WHO growth reference and the MGRS growth standard

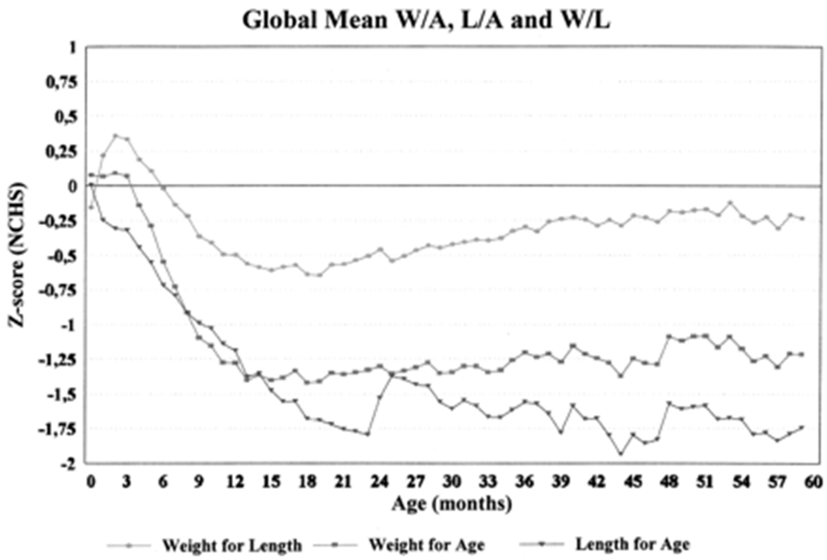
Patterns of child growth are most commonly described in comparison to age and sex specific references or standards. Before 2006, the World Health Organization (WHO) promoted the international use of the U.S National Center for Health Statistics (NCHS/WHO) growth reference. Over time, however, various criticisms of the NCHS/WHO reference emerged, namely that it was based on a largely bottle-fed U.S. population of infants. Support for this criticism grew as it became widely recognized that healthy bottle-fed infants grow very differently than breastfed infants in the first 12 months of life [8]. Use of the NCHS/WHO reference in populations such as those in South Asia where most infants are breastfed for long periods of time results in substantial risk for misclassification of infants into abnormal weight and length gain categories [8, 9]. The Multicentre Growth Reference Study (MGRS) was thus designed by the WHO to reflect optimal conditions for child growth. Children were selected for this study because they were exclusively breastfed until at least four months of age and, lived in environments from six countries where growth was unlikely to be constrained. The measurement interval was also sufficiently frequent to better reflect the dynamics of growth during this period. The MGRS more closely resembles a growth standard, in that it makes a prescriptive statement about how children should grow, and necessarily shifts the previously accepted boundaries to define undernutrition [8].

In 2010, Victora and colleagues conducted an analysis of datasets from 54 countries using the MGRS growth standard for calculation of weight-for-age (WAZ), length/height-for-age (LAZ/HAZ) and weight-for-length/height (WLZ/WHZ) Z-scores. This analysis showed that when child growth was compared to the MGRS standard, growth faltering was more pronounced and began earlier than when the NCHS/WHO reference was used for comparison [10] (**Figure 1**). LAZ showed a similar timing and degree of faltering when either reference was used, but WAZ, in contrast, fell below the MGRS growth standard median starting from birth and, plateaued at a Z-score value closer to the median. The consequence of this earlier weight faltering is that WLZ also declines earlier in life, by three rather than six months of age [10, 11]. Various country specific analyses using the MGRS growth standard rather than the NCHS/WHO reference have demonstrated that due to these shifts in growth patterns, prevalence estimates of undernutrition have significantly increased during infancy, with the largest increases occurring between birth and six months of age [9, 12, 13]. Recent analyses suggest that the prevalence of wasting based on comparison to the MGRS growth standard is strikingly higher than estimates derived using the NCHS/WHO growth reference [9, 13-15]. These observations do not support the previously held assumption that undernutrition during the first six months of life is of less concern compared to the 6-24 month period.

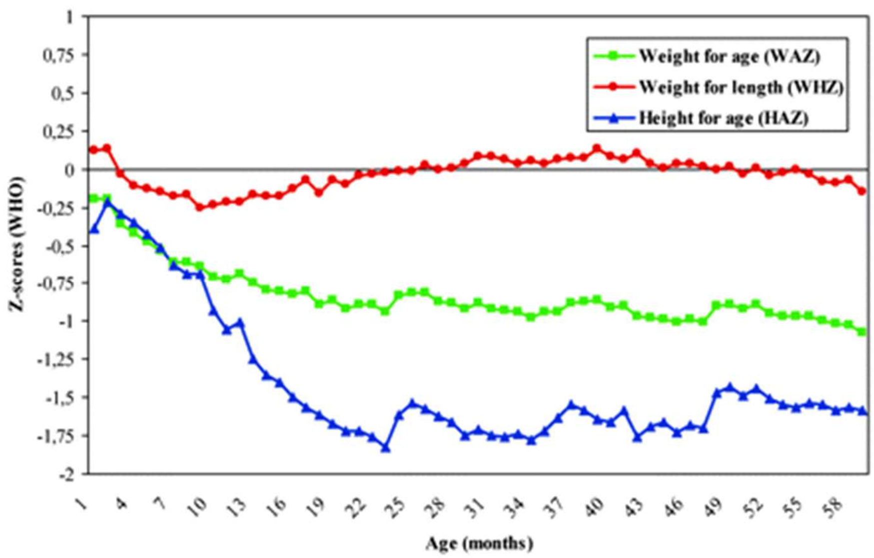
1.4 The first "500 days"

1.4.1 The first "500 days" are a critical period

As a subset of the first "1000 days", the first "500 days" (the period from conception to approximately six months of age) is a precarious time for growth and development, especially in developing countries. Fetal and early infant health and nutritional status are intricately linked with the status of the mother, and are affected by a complex interplay of factors during both the pre- and postnatal periods [16]. Small-for-gestational age (SGA; weighing less than the 10^{th} centile of birthweight-for-gestational age for a sex specific reference) is a commonly used proxy for intrauterine growth restriction (IUGR) [17]. In developing countries where the prevalence of SGA is high, IUGR is the most likely cause [17, 18]. SGA infants have a higher risk of both morbidity and mortality in both the neonatal and later postnatal periods [19, 20]. If they do survive, they are also more likely to remain small throughout infancy and even childhood, especially in poor environments where substantial catch-up growth is unlikely (a return to a "normal" growth trajectory) [21, 22]. Appropriate-for-gestational age infants (AGA; weighing greater than the 10^{th} centile of birthweight-for-gestational age for a sex specific reference) are also at high risk for growth faltering in early postnatal life if they are faced with persistent exposure to a poor environment and reliant on mothers who experience nutritional deficits and time limits for childcare. Poor growth established in early life is an important predictor of poor growth and undernutrition in later childhood [21-23].



(A) Worldwide timing of growth faltering based on the NCHS/WHO growth reference (solid line represents the NCHS/WHO reference median). Height-for-age Z-scores are length-for age Z-scores for children measured above two years of age [11]



(B) Worldwide timing of growth faltering based on the MGRS growth standard (solid line represents the MGRS standard median). Height-for-age Z-scores are length-for age Z-scores for children measured above two years of age [10]

Figure 1.1 Worldwide timing of growth faltering based on NCHS/WHO growth reference (A) and MGRS growth standard (B)

1.4.2. Undernutrition in the first "500 days" in India

In India, IUGR represents a large public health burden. Nearly 50% of all SGA infants are born in South Asia, and India is the largest contributor to this burden (36.5% prevalence of SGA in India) [19]. Undernutrition during infancy is also rampant. One analysis of Indian nationally representative cross-sectional data using the MGRS growth standard for comparison, estimated that 20.4%, 30.6% and 29.6% of infants are stunted, wasted and underweight, respectively between 0-6 months of age. Wasting was 31% higher in infants 0-6 months of age as compared to infants 6-59 months of age [12].

1.4.3 Determinants of growth during the first 500 days

In the early 1990's The United Nations Children's Fund (UNICEF) developed a conceptual framework for understanding the determinants of undernutrition, which has since been used as the basis for the development of various other nutrition frameworks (**Figure 1.2**) [24]. The key factors that influence childhood undernutrition can be summarized as basic, underlying and immediate causes. Basic causes include factors such as resources in the environment and the way they are controlled. Underlying causes deal with factors at the household/family level and include the various aspects of behaviors and practices related to food, health and care. Underlying causes have a direct effect on the most immediate causes of undernutrition at the individual level: inadequate dietary intake and disease. Of importance are the complex and bi-directional associations between these various factors, represented by double sided arrows in the conceptual framework. Although the UNICEF framework was designed more broadly for children less than five years of age, it is a simple heuristic tool that can be used to understand the general factors that affect growth and nutritional status during the first "500 days".

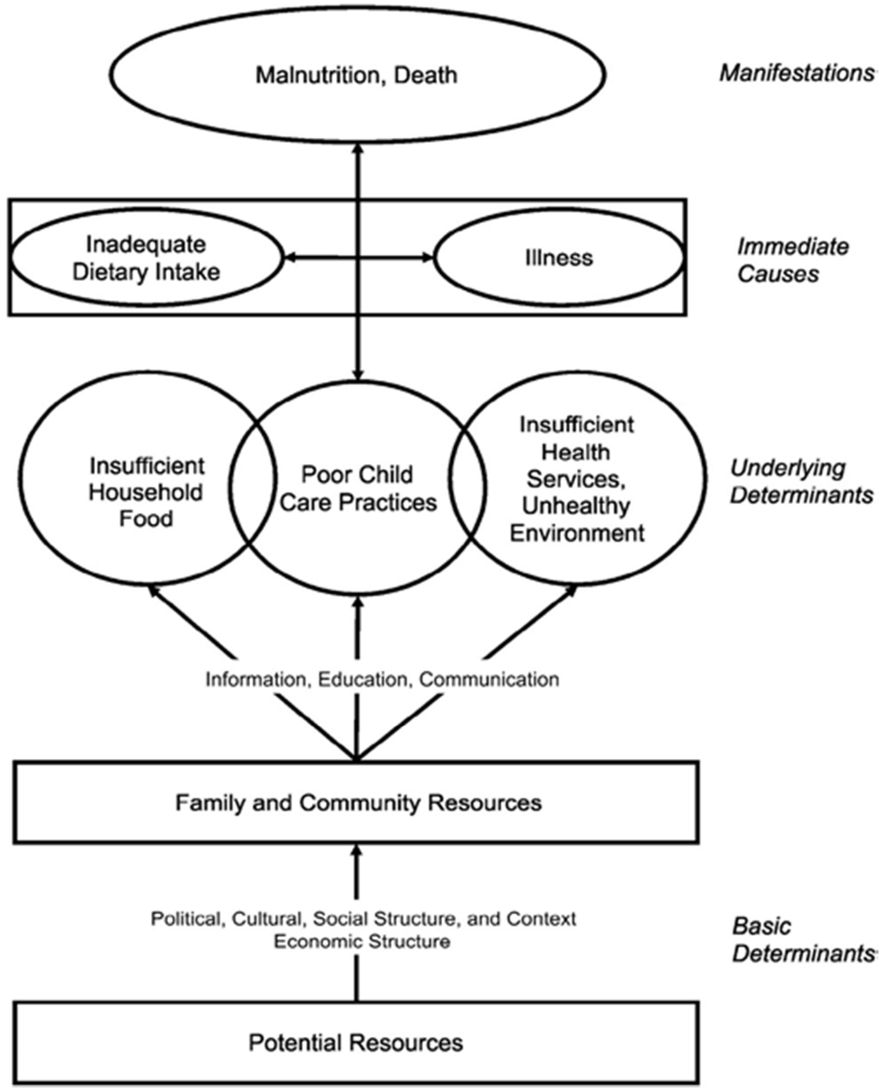


Figure 1.2 The UNICEF conceptual framework [24]

Growth in early life is affected by a complex interplay of factors involving both *in-utero* and postnatal determinants. The first “500 days” represent a critical period within the first 1000 days when the infant is entirely dependent on the mother for nourishment via the placenta and breastfeeding [16]. Maternal health and nutritional status during this period is thus particularly important. Poor health and nutritional status, limited access to healthcare and services, inadequate dietary intake and excessive physical labor demands during pregnancy have been associated with a variety of poor fetal growth outcomes in low resource environments, including low birth weight (LBW) and SGA [16, 25-42]. Small size at birth has been associated with a host of short and long-term unfavorable consequences, such as increased infant morbidity and mortality and poor growth in later life [3, 28]. SGA infants who are faced with persistent health insults in postnatal life (e.g. via unsanitary environment) are unlikely to experience any “catch-up” growth, or a return to a normal growth trajectory [17, 21-23, 43]. Some evidence also suggests that compared to AGA infants, LBW and SGA infants are born with different nutrient requirements, which if not addressed, will place the infant at further risk for poor postnatal growth and development [2, 44]. Maternal biological risk factors also have a complex interplay with cultural beliefs and practices. For example, in many agricultural communities, the concept of rest during pregnancy may be non-existent. During periods of peak agricultural labor demands, a pregnant woman may work in the fields until delivery, further compromising her health and nutritional status, and potentially adversely affecting fetal growth [40, 41, 45-47].

Recent research in various developing countries indicates that only 50% of infants that are undernourished (wasted) between birth and six months of age are reported as small at birth, indicating that although prenatal factors are an important determinant of growth faltering in the first six months of life, postnatal factors also play a key role [13]. In the early postnatal period, maternal health and nutritional status continues to be an important determinant of infant growth and development [16, 28]. Although the extent to which maternal undernutrition affects the quantity and quality of breast milk is still debated, poor maternal nutritional status is likely to negatively affect quality aspects of infant care and feeding [48-54]. In the early postnatal period, infants are newly exposed to various environmental pathogens that vary according to physical location, time constraints (e.g. via work demands) and other maternal behaviors and practices (e.g. feeding behaviors, childcare practices, etc.) [55-59]. Health services for women and young children in rural areas of developing countries are often of poor quality, and access may be unreliable [60-64]. Substantial literature documents that breastfeeding, and particularly exclusive breastfeeding promotes better infant growth, and current WHO recommendations are for exclusive breastfeeding until six months of age [64-68]. In many developing countries, however, breastfeeding behaviors do not meet these guidelines, which may expose infants to a greater risk of infectious disease and inadequate nutrient intakes [69]. Inadequate feeding practices are potentially important explanatory factors for why high levels of undernutrition exist, even in the infant who consumes some breast milk [13].

1.5 Special considerations for rural populations

1.5.1 Nutrition and agriculture linkages

Within India there is well-recognized heterogeneity in the prevalence of undernutrition between urban and rural areas. Prevalence estimates of undernutrition for children less than five years of age in rural India are 41.2%, 21.5% and 38.3%, as compared to 31.0%, 20.0% and 29% in urban Indian, for stunting, wasting and underweight, respectively [6]. The vast majority of the poor continue to reside in rural areas and remain largely dependent on subsistence and semi-subsistence agriculture [70]. The agriculture sector employs almost 58% of the total Indian workforce and, more than 80% of rural women in the work force are involved in agriculture [70]. Recent literature reports a “feminization” of agriculture in India and many studies suggest that rural women consistently work more hours than rural men. In addition, rural women have a direct influence on the health and well-being of their children during both the pre- and post-natal periods through their own nutritional status, as well as their ability to manage the feeding and care of young children [47]. Consequently, women’s involvement in agriculture has been identified as a factor with potentially important implications for both maternal and child health, and is considered as a critical linkage between nutrition and agriculture [47, 71].

1.5.2 Seasonality

In tropical and sub-tropical regions of developing countries, often-extreme variations in the weather (e.g. temperature and rainfall) delineate different “seasons”, or periods of the year [72]. In rural areas, local and regional weather patterns and agro-ecological conditions (biophysical environment) in turn drive the agricultural cycle, including agricultural production. Agricultural production may in turn feed back to affect various aspects of the biophysical environment (e.g. via soil degradation, use of water and pesticides etc.), as well as community and household resources (e.g. employment, income, health, locally produced food, etc.) [70-72]. The term "seasonality" is in turn used to describe any regularly occurring variation that is correlated with the seasons (e.g. agricultural seasonality, growth and nutrition seasonality, etc.), and is a key feature of rural lives and livelihoods [72].

1.6 Seasonality of child growth and undernutrition in developing countries

In rural areas of low-income countries, seasonality, or seasonal variation in growth, is usually attributed to underlying seasonal variation in factors such as food availability and infectious disease [72, 73]. It is generally accepted that a convergence of risk factors for poor health and nutritional status (e.g. diminished household food supplies, high demands for agricultural labor, increased exposure to disease vectors in the environment) during high-risk periods of the year largely account for observed seasonal variation in undernutrition [72-74]. In rural agrarian populations, where chronic extreme poverty is often the norm, seasonal stress may exacerbate the already poor health and nutritional status of vulnerable groups, and thus serve as an indirect driver of growth failure in young children [75].

1.6.1 Proposed mechanisms: seasonal variation and child growth

Early child growth has been a focus of investigations for many years, yet the exact biological mechanisms that govern infant growth, particularly linear growth, remain poorly understood. In early childhood, it is known that nutrient stores, nutrient losses, diet quality and overall health status have key influences on growth. Children exposed to nutritional insults, such as those associated with seasonal stress in poor environments, will frequently be in physiological states that involve overall deficiency of key nutrients as well as low absorption and high losses of nutrients. Inflammation also likely plays an important role in the growth process [76, 77].

The specific mechanisms driving growth failure at both the cellular and whole body levels are still debated, but it is widely accepted that the process of normal growth starting from birth until puberty is under the influence of growth hormone. Some evidence, however, also supports an independent effect of insulin-like growth factor (IGF-1) [78, 79]. In response to the release of growth hormone, IGF-1 is released at active sites of bone growth, which promotes increases in both muscle and bone mass. In the undernourished child, levels of growth hormone increase, but the activity of IGF-1 decreases. Lipolysis and oxidation of fat in the absence of bone and muscle growth is an important glucose sparing adaptation for meeting central nervous system requirements [80, 81]. Leptin, a hormone synthesized by adipocytes, may also be involved in the bone metabolism that occurs during the growth process [82, 83]. Studies to suggest that weight gain tends to precede increased linear growth have also prompted additional thinking about the potential role of nutrient signaling and its relationship to adipose tissue in the human growth process [84, 85].

Additional research is needed to clarify the proposed mechanisms underlying the biology of child growth and growth failure, and to better understand the potential to recover from growth failure. Young children appear able to recover to various degrees from a period of growth faltering. In healthy environments, children less than two years of age may even experience “catch-up growth”, or a return to their normal growth trajectory [43, 86, 87]. In poor rural settings, however, conditions for adequate nutritional recovery are unlikely to be present [73, 88, 89]. Consequently, growth faltering associated with seasonal stress is likely to persist, even in more favorable periods of the year. Even if some nutritional recovery is attained, exposure to the next high risk period may again lead to declines in nutritional status, the result of which is a vicious cycle of undernutrition and inadequate nutritional recovery.

1.6.2. Seasonal patterns of child growth

In poor rural communities of developing countries, differences in attained size and rates of growth throughout the year is a phenomenon that has been fairly well documented for older children, but less so for children under six months of age. With some exceptions (e.g. by month/s of year, by specific climatic factors, etc.), the prevailing seasonality and child growth literature describes seasons of the year based largely on agro-climatic factors (e.g. summer, winter, rainy/monsoon, harvest, etc.). In different locations, even within the same country, specific months of year may correspond to different seasons and/or timing of agricultural events, resulting in some challenges for cross-context comparisons. The over-arching pattern that emerges in rural areas of developing countries, however, is one of declining child nutritional status in the months of year corresponding to the heavy rain period, or "rainy" season, and improving nutritional status during the post-harvest period (usually autumn/winter) [72, 74].

In rural populations in both Africa and Asia, higher birthweights are often observed during the late rainy and pre-harvest ("hungry") seasons, often resulting in monthly or seasonal differences throughout the year of greater than 100 g [45, 90-92]. Studies conducted in the Gambia, India and Bangladesh reveal maximum birthweight differences between months of the year of approximately 500 g, 145 g and 50 g, respectively [45, 92, 93]. In analyses, however, these studies did not all control for the same, or any, potentially confounding variables, which may explain the large differences in observed magnitudes between countries. In contrast to birthweight, seasonality in birth-length is less well documented. A few studies, however, have shown differences as great as 0.5-1.0 cm between months of maximum and minimum birth-lengths. In a rural population in Maharashtra, India, differences in birth-lengths from month to month were observed to be lowest in the winter months (January) and highest in the summer months [45]. In Bangladesh, lower birth-lengths were also observed in the winter months (November-January). Infants born in the winter months in these settings would have experienced their second trimester of pregnancy, the period when the rate of fetal linear growth is thought to be greatest [94], during the late rainy and pre-harvest periods. One study in the Gambia showed that the incidence of SGA was highest at the end of the hungry season (August-December), and lowest in June, a pattern that differed from that of the births of pre-term infants [95].

For the postnatal period, literature from developing countries reveals a general pattern of increased growth faltering and increased prevalence of undernutrition that occurs during the rainy season as compared to the dry, post-harvest period. Inadequate reporting and the use of different growth references across studies, however, prevent direct comparison of the magnitudes of these effects. In Bangladesh, a 3-4-fold difference in the percentage of expected monthly gain in infants 6-60 months of age was observed in different months of the year (worst during the rainy season and harvest period). This study also demonstrated that incremental changes in the undernutrition indicators, weight-for-age and weight-for-length, reflect seasonal declines more rapidly than do prevalence estimates of undernutrition [96]. In the Gambia, seasonal fluctuations as a percentage of the overall sample mean value in weight and length were observed for children from 0-24 months of age. Fluctuations were relatively larger for older children and for weight (9% at one month of age and 13% at 11 months of age for weight). Seasonal fluctuations in rates of weight and length growth showed a more consistent pattern at all ages and occurred earlier than fluctuations in achieved weight and height. The association of the rainy and pre-harvest season with growth was also shown to depend on the month birth. Those born in the winter and pre-monsoon seasons did relatively better than those born at other times of the year, indicating a possible interaction between prenatal factors and postnatal environmental exposures on postnatal growth [73].

In Taiwan, a longitudinal study was designed to explore the association between season and incremental weight changes in four cohorts of infants born during four different seasons. The highest and lowest increments in weight occurred in the winter and summer months, respectively, except for infants in the first period of incremental growth (0-3 months old). In this group of infants, there was no association between season and rate of weight growth after controlling for birth-length and weight. After three months of age, however, the association of season with rate of weight growth became significant. These findings highlight the potential differential association of season with growth depending on the age of the infant during exposure [97].

In another population-based cohort of children 0-36 months of age in Malawi, an age-specific seasonal pattern in rate of weight and length growth was also observed. Among one to six months old infants, both WAZ and LAZ declined most rapidly in the rainy season as compared to the non-rainy season. For the group of infants aged 7-12 months, no seasonal pattern of incremental growth was observed [98]. The differences in findings between this study in Malawi and the previously described study in Taiwan could be a reflection of sampling differences. They could also reflect possible differences in the coping strategies employed in different populations that depend on the age of the infant. Alternatively, these differences may suggest that vulnerability to seasonal risk factors is age-dependent. Many important questions about the seasonal dynamics of infant growth remain, especially for infants less than six months of age.

1.6.3 Re-thinking seasonality research

Despite prevailing explanations for observed differences in child growth patterns throughout the year, analyses of child growth have been largely centered on somewhat arbitrary climate-based definitions of seasons. Devereux and colleagues question this climate-based approach based on evidence from wealthy countries that cycles in the weather do not translate into seasonal fluctuations in the same way as they do in poor countries (e.g. food availability, food prices, consumption, etc.). These authors argue that "poverty, not the weather is the binding constraint" and call for increased attention to the issues of access and distribution that may vary by location, socio-economic status, gender, and a host of other factors [72]. Overall, chronic poverty sets the stage for undernutrition that may be exacerbated by regularly recurring seasonal stress. Available literature points to the rainy season as an especially important period for seasonal stress. It is not, however, the rainy season weather *per se* that directly impacts health and nutritional status. Rather, the rainy season represents a multi-faceted system in which impoverished and nutritionally vulnerable individuals and populations are exposed to increased risk factors for poor health and nutritional status (e.g. infectious disease, low household food supplies, etc.) [75]. Chambers utilizes the term "integrated seasonal poverty" to describe the interconnectedness of the various components of seasonal stress, factors that are not necessarily restricted to the rainy season alone [75]. The immediate and underlying determinants of undernutrition, as summarized in the UNICEF conceptual framework, are integral components of "integrated seasonal poverty." Therefore, theoretically, it is not the weather or season that has a direct effect on young child nutritional status, but rather fluctuations in the proximal determinants of health and nutritional status throughout the year. Changes in these determinants throughout the year, however, are poorly understood, especially as they affect the health and nutritional status of young infants.

1.7 Seasonal variation in the immediate and underlying determinants of undernutrition in early life in South Asia

Seasonal differences in risk factors for undernutrition is likely to be highly context specific. Therefore, the research literature was searched to examine whether evidence exists for seasonal differences in the immediate and underlying determinants of undernutrition during the first "500 days" in rural South Asia.

1.7.1. Season and child feeding and care

A few published research studies were found that illustrated seasonal differences in breastfeeding and breastfeeding practices in rural South Asia, but no studies were found that examined seasonal differences in childcare practices. Brown and colleagues estimated breast milk consumption via test weighings in a longitudinal study of children aged 5-18 months in rural Bangladesh [99]. Breast milk intake in October-November was lower than in April-May, and only approximately 88% of the age expected amount ($p<0.005$). The authors suspected this decrease to be a reflection of reduced maternal lactation capacity [99]. In contrast, two studies, examined the seasonality of breastfeeding practices. In India, the odds of children aged 0-5 months being exclusively breastfed (EBF), or the odds of infants aged 6-8 months having received EBF for the recommended duration (six months) were greater in winter compared to non-winter months ($p<0.05$) [100]. Panter-Brick and colleagues also found evidence of seasonal differences in nursing behaviors in children 1-38 months of age that varied by ethnic group [101]. In Nepal, for one ethnic group (Kami), but not the other (Tamang), significant seasonal differences were observed for nursing interval ($p<0.05$), frequency ($p<0.01$) and mean feed duration ($p<0.001$) in favor of increased mean time, increased frequency and decreased interval in the monsoon season compared to other seasons [101]. Authors reported that these findings were somewhat unexpected due to the heavy work demands that were observed for women during this period. Seasonal differences in breastfeeding may depend on biological factors related to the mother and infant, as well as cultural beliefs and practices, such as work during lactation [101].

1.7.2. Season and morbidity

A differential seasonal burden of infectious pathogens is a well-documented phenomenon in many areas of the developing world. During the rainy season, high humidity and temperature increase the growth of pathogens that are frequently implicated in diarrhea cases. The incidence of waterborne pathogens and intestinal parasites is also substantially increased. Furthermore, the rainy season is the peak-breeding season for mosquitoes, which increases the risk for mosquito borne illnesses including malaria and dengue fever. In the dry season, respiratory infections, diarrhea caused by rotavirus, and scabies have a tendency to peak [74, 102]. In various settings including India, the monsoon season has been associated with a range of illnesses including gastrointestinal infections, malaria, tuberculosis, measles and whooping cough [75, 103, 104].

A few studies were identified that provided some evidence for seasonal differences in diarrhea and acute respiratory infection (ARI), two of the most important illnesses affecting infants during the first six months of life. In one study of 4-27 month old Bangladeshi infants, Zeitlin and colleagues demonstrated that the incidence of diarrhea was highest in the hot and dry months of April and May compared to other months ($p < 0.001$) [105]. In another study in rural Bangladesh, compared to the winter season, Pathela and colleagues showed that both spring and summer were significantly associated with an increased risk of diarrhea in children 0-2 years of age ($p<0.001$ and $p<0.05$, respectively) [106]. In contrast, in rural India, in a sample of neonates (1-28 days of life), Bang and colleagues reported no significant seasonal difference in the incidence of diarrhea [107]. This lack of seasonal variation may suggest that infants in the first month of life are relatively buffered from the seasonal effects of diarrhea, perhaps due to the protective effects of breastmilk and/or less exposure to environmental contaminants as compared to older infants [107]. In this study, however, seasonality in ARI was observed. Compared to other seasons, rates of ARI were reported to be significantly higher in the winter months ($p<0.05$) [107]. Rupa and colleagues observed a similar seasonal pattern in Indian infants 0-12 months of age. In contrast, in Bhutan, in a sample of slightly older infants (13-36 months of age), the incidence of ARI was significantly higher in the monsoon season relative to other seasons ($p=0.027$) [108]. Seasonal patterns in morbidity in young infants are likely to differ based on the types of pathogens present, and may vary depending on infant age, even during the first six months of age.

1.7.3. Season and maternal health and nutritional status

The health and nutritional status of mothers during pregnancy and lactation is integrally important to the health and development of the child, as previously described. Among pregnant women in a longitudinal study in rural India, median energy and protein intakes were significantly higher in winter (September-January) as compared with summer (February-May; p=0.001) [45]. Similarly, in rural Bangladesh, diet diversity scores were significantly higher in the late autumn months (October-December) as compared to other months ($p<0.05$) [109]. From the same study, household food insecurity scores were significantly lower in the monsoon period [109]. One study of dietary intake in a combined group of pregnant and lactating women from rural India, also suggested a negative association between the median intake of nutrients and the monsoon season [110]. Seasonal variation in these determinants of nutritional status are likely to depend on the aspect of diet measured, as well as the context specific patterns in food availability and access.

1.7.4. Season and maternal work and physical activity

Although not included as an immediate determinant of undernutrition in the original UNICEF conceptual framework, high maternal energy expenditure is a proxy for heavy physical exertion, and is an important component of energy balance for women who are integrally involved in agricultural labor. High energy expenditure is also a proxy for time spent in strenuous activities, activities which may detract from time spent in activities such as child care [111]. Two prospective studies from Nepal and India reveal some evidence for seasonal differences in energy expenditure. In rural Nepal, Panter-Brick and colleagues estimated energy expenditure for pregnant and lactating women. The authors reported that regardless of pregnancy or lactation status, women had significant seasonal increases in total energy expenditure and time spent in outdoor subsistence work from January-March (late winter) to July-September (monsoon) ($p<0.009$ and $p< 0.018$ for non-pregnant, non lactating women and pregnant and lactating women, respectively) [46].

In India, Rao and colleagues similarly showed significant seasonal differences in maternal activity during pregnancy. In contrast, however, the highest and lowest median activity scores occurred in October (winter) and June (monsoon), respectively ($p<0.001$) [45]. The differences in findings from these studies may be attributed to several factors, including differences in measurement techniques, sample size and analytical approach. It is also possible, however, that the observed seasonal differences in these populations reflect underlying differences in social determinants (e.g. beliefs about work and rest during pregnancy and lactation) or other seasonal factors driving labor demands, such as difference in timing of peak work demands for women [40].

1.8 Conceptual framework and specific aims

Based on the review of the literature, a conceptual framework (**Figure 1.3**) was developed to illustrate the hypothesized relationships between months of conception, size at birth and early postnatal growth. In brief, month of conception is hypothesized to affect fetal growth, and by proxy, early neonatal size (measured here between zero and seven days), via effects on the nutritional status of the mother (MNS) during pregnancy. MNS is determined by more distal factors such as pre-conception nutritional status (height) and socio-demographic status, and by more proximal factors including maternal diet (food security as a proxy), work demands and morbidity. MNS during lactation is part of a continuum and reflects pre-conception MNS and MNS during pregnancy. It also reflects maternal diet (food insecurity as a proxy), work demands and morbidity during the lactation period. Infant size at birth is also determined by more proximal factors including length of gestation, parity, and sex of the infant.

In the postnatal period, it is hypothesized that prenatal variables (the effects of which are represented by size at birth) will continue to be determinants of rates of postnatal growth. Similar to the prenatal factors that are linked to month of conception and length of gestation, postnatal growth is determined in part by the time (specific months) of year during which postnatal growth is assessed. The month of year starting the growth interval is hypothesized to affect maternal and infant factors (e.g. breastfeeding, care and morbidity), which in turn also determines rates of postnatal growth during the first six months of age. Based on the review of literature and factors summarized in Figure 1.3 this dissertation addresses three specific aims through study of mothers and infants from a rural agricultural region in Uttar Pradesh, India.

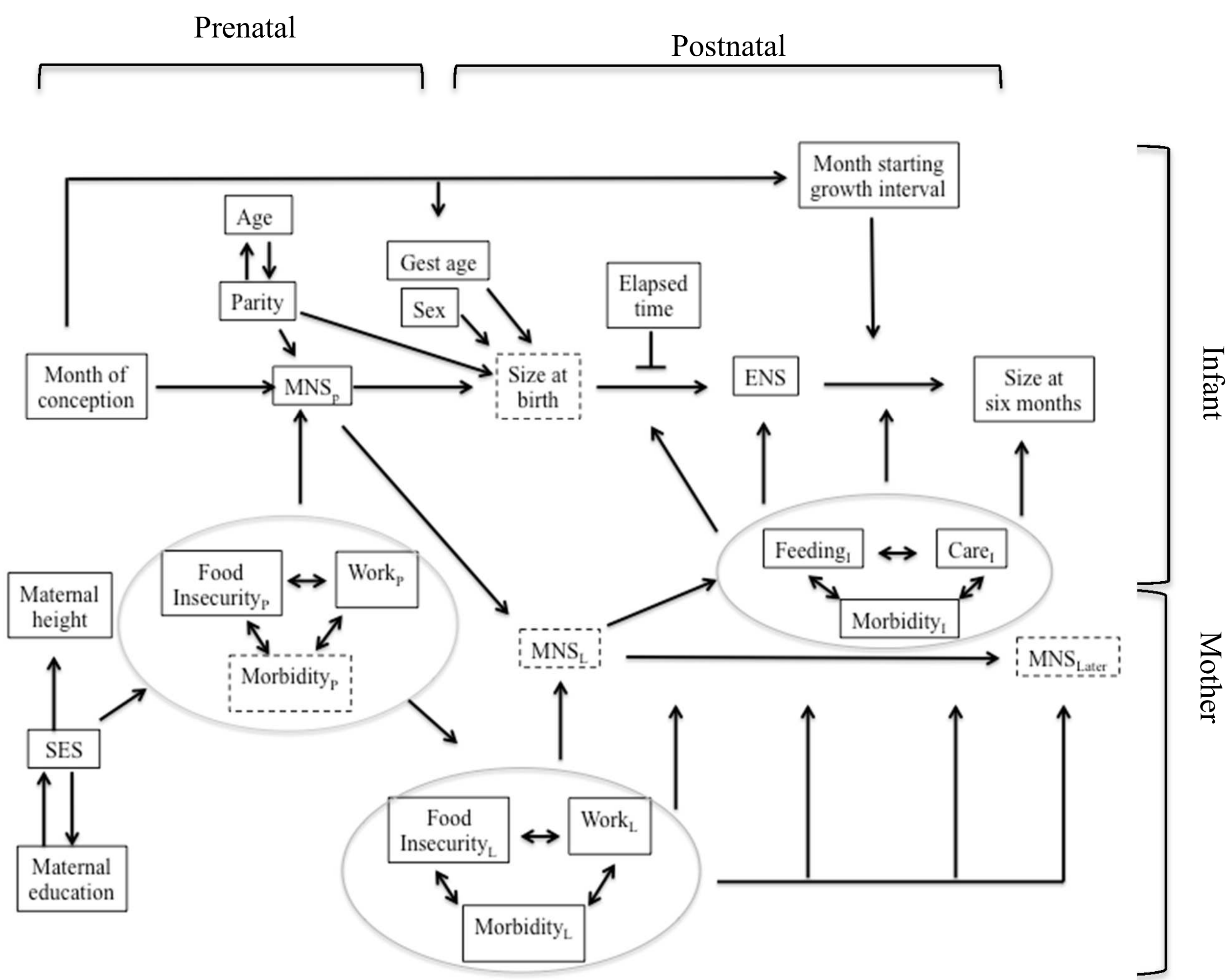


Figure 1.3 Conceptual framework for the present research[123]

[1] P, L and I superscripts represent pregnancy, lactation and infancy
[2] Momonths; MNS:maternal nutritional status; Work: time spent in agricultural labor; gest age: gestational age; ENS: early neonatal size
[3] Variables inside dashed lines represent variables not measured in the present research

Specific Aim 1: To describe differences in early neonatal body size by month of conception and to identify prenatal risk periods for fetal growth faltering. This will be achieved by relating month of conception to early neonatal size (weight and recumbent length) while controlling for potential confounding by fixed, or time invariant infant (sex. gestational age and postnatal age), maternal (height, parity, education) and socio-demographic variables (socio-economic status).

Specific Aim 2: To ascertain the typical growth patterns of recumbent length and weight (attained size and rates of growth) throughout the first 6 months of life, and the relationship of these growth patterns to the month of year representing the beginning of the growth interval. This will be achieved by analyzing serial infant growth data by infant age and month of year for infants between birth and six months of age.

Specific Aim 3: To examine the association of time-independent maternal and infant factors, time-dependent infant postnatal and maternal postpartum characteristics and season with rates of weight and length growth from 1-4 months of age. This will be achieved by relating data on season, maternal and infant prenatal characteristics (maternal height, primiparity, newborn size, village), infant postnatal factors (breastfeeding, childcare, morbidity and vaccination) and maternal postpartum factors (time spent in agricultural work, diet diversity, nutritional status, food insecurity and morbidity) with infant growth velocities from 1-4 months of age.

1.9 Significance and justification for the study

Undernutrition remains a large problem in much of the developing world, particularly in India. Moreover, the introduction of the MGRS standard has highlighted that the magnitude of the problem in infants less than six months of age is much larger than previously thought. Nationwide cross-sectional data from India has indicated a 30% prevalence of wasting in infants 0-6 month of age [9, 13]. Reliable growth data, especially to determine rates of growth, for the most nutritionally vulnerable infants in rural India, however, are limited. As a result, the predisposing factors and mechanisms leading to the process of growth faltering are poorly understood, particularly in breastfed infants [13, 16].

Rural Indian mothers and infants are among those most vulnerable to undernutrition and to seasonal stress [112]. Research to understand seasonal growth dynamics in young infants, especially in South Asia, however, is lacking. Available seasonality research is largely climate-centered, but some limited evidence illustrates seasonal differences in known risk factors for poor infant growth and undernutrition in rural South Asia. There is, however, a dearth of published research to examine the inter-relationship between season, risk factors for poor growth and undernutrition and rates of growth during the first six months of life. "Integrated seasonal poverty" may occur at different periods of the year in different populations, or may cycle throughout multiple periods of the year [113]. Seasonal stress is likely to become increasingly unpredictable in future years due to the effects of factors, such as climate change [114]. A more holistic understanding of differences in risk factors for poor health and nutritional status throughout the year will allow researchers and policy makers to better understand implications of month or season of the year for nutrition sensitive and specific programs and policies.

Chapter 2
Methods

2.1 Longitudinal growth study design

This was a longitudinal study of infant growth with continuous recruitment of participants. From July 2014 to September 2015, all eligible pregnant women in the 32nd week of pregnancy or later, residing in nine villages in the Shivgarh block of the Rae Bareli district of the Indian state of Uttar Pradesh were invited to participate in the study (**Figure 2.1**).

Figure 2.1 Villages of the Shivgarh Block, and villages selected for inclusion in the longitudinal study [115]

The objective of the continuous recruitment and serial measurements was to assure that 12 monthly birth cohorts would be recruited in which infants would have different monthly exposure at different ages during the first six months of life. The additional months of recruitment after June 2015 were included to compensate for slow recruitment that occurred at the onset of the study. Pregnant women, who accepted participation and signed informed consent were enrolled in the study and scheduled to be visited a total of eight times: during late pregnancy (enrollment), at birth (within seven day), and then monthly (±14 days) between one and six months of infant age (**Figure 2.2**). As part of a larger study outside the scope of this dissertation, these same infants were visited two more times, at nine and 12 months of infant age (± 14 days). The final six-month visitation for mother-infant pairs enrolled in the study occurred in April 2016. At each visit, a structured questionnaire was administered to the pregnant women and head of the household, or other knowledgeable household member, by six trained and standardized survey enumerators, working in pairs, to collect detailed household, maternal and infant information. Maternal and child anthropometry were also collected at each visit by the same six enumerators. Copies of the English version of the survey modules are found in Appendix A. Both the International Food Policy Research Institute (IFPRI) and the Community Empowerment Lab (CEL; local collaborating organization) ethical review boards provided ethical approval for this study.

2014						2015												2016			
Jul	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**
P	B	1	2	3	4	5	6	6													
	P	B	1	2	3	4	5	6													
		P	B	1	2	3	4	5	6												
			P	B	1	2	3	4	5	6											
				P	B	1	2	3	4	5	6										
					P	B	1	2	3	4	5	6									
						P	B	1	2	3	4	5	6								
							P	B	1	2	3	4	5	6							
								P	B	1	2	3	4	5	6						
									P	B	1	2	3	4	5	6					
										P	B	1	2	3	4	5	6				
											P	B	1	2	3	4	5	6			
												P	B	1	2	3	4	5	6		
													P	B	1	2	3	4	5	6	
														P	B	1	2	3	4	5	6

Figure 2.2 Flow of women and infants from study recruitment until the six-month follow up visit[4]

[4] P= recruitment/pregnancy visit at 32nd week of pregnancy or later, B=birth visit; 1-6= age of infant in months (±14 days) at monthly follow-up visits

2.2 Study participants

The Rae Bareli district is located approximately 70 km from the capital city of Lucknow. In 2015-2016, the prevalence estimates of child (less than five years of age) undernutrition were 36.1%, 32% and 42.2% for stunting, wasting and underweight, respectively [116]. Shivgarh consists of 39 villages, and for this study nine villages were purposefully selected by CEL field managers with in-depth knowledge of the local area to be representative of the regional variability (e.g. agriculture and socio-economic status) of the Shivgarh block, located approximately equidistant from the CEL Shivgarh field office (**Figure 2.1**), and to have a sufficient number of births each month to meet sample size objectives.

The climate in Shivgarh is subtropical, and generally characterized according to three seasons: summer (April-June), monsoon (July-September) and winter (October-March). Day/night temperatures can exceed 40 degrees Celsius in summer months (highest mean temperature in May), and reach lows of nearly ten degrees Celsius in winter months (nadir in January). Rainfall occurs primarily between July and September (highest mean rainfall in August), with negligible rainfall during other months of the year [117]. Between May and August 2013, formative research was conducted in Shivgarh to understand local seasonal patterns, the agricultural cycle and general childcare and feeding practices (**Appendix A; Table 2.1**). In addition to the generally recognized climate-based seasons, seasons are also frequently described according to the agricultural cycle as rice, wheat and peppermint, corresponding to the crops grown during the monsoon, winter and summer periods, respectively. The primary livelihoods in Shivgarh are semi-subsistence farming and hired agricultural labor, and most farmers have access to irrigation via canals and tube wells. The staple crops in this area are rice and wheat, and peppermint is grown as a cash crop. Mustard seed and some vegetables may be grown as inter-crops with the wheat crop, and if land is available, some vegetables (e.g. potato, spinach, etc.) may also be grown. When famers own land, however, they are typically small plots of land (less than one hectare).

Women are integrally involved in almost all aspects of agricultural work including transplanting rice, sowing rice and wheat, field maintenance (e.g. weeding, watering), harvesting of crops, post-harvest processing (e.g. rice threshing), but do not typically engage in land preparation activities (e.g. plowing). Although other types agricultural activities are ongoing throughout the year, women reported that the heaviest labor demands occur between March and July, corresponding to the sowing and harvesting periods for rice and wheat, respectively. Pregnant women reported working in the fields through the 7th month of pregnancy or later. A confinement period after delivery is common and typically lasts between seven and 20 days. After this period, women return almost immediately to household work. The duration of rest that women report taking from agricultural tasks after delivery, however, is more variable. Most women will resume agricultural work within 15 days to one month, but a few participants reported no agricultural work for nearly six months after delivery. Women do not report taking the infant to the field while they work and, young infants are usually left in the care of an older child, or grandparent. If women are breastfeeding, they report returning from the field throughout the day to feed the infant. The introduction of animal milks and water is common practice, especially during the hot, summer months. Mothers report that diarrhea and fever are common in young children, especially during the monsoon.

Participants in the formative research did not report a "hungry" season, but described the period from July to September as a risk period for low food availability due to diminishing supplies of wheat that may occur while the rice crop is still in the field. Immediately after harvest, men and/or the head of the household decide how much of the crop to store or sell, and so the quality of the harvest is likely an important determinant of whether a "hungry" season emerges during the year. The Public Distribution System, a social support program that supplies subsidized grains and other supplies (e.g. sugar, kerosene, etc.) to the poor is semi-functional in Shivgarh, but the usage of the system in sporadic because of the quality of the grains is reportedly poor. This program, however, may serve as an important mitigating factor for seasonal food shortages.

For this study, pregnant women were identified via CEL's pre-existing pregnancy surveillance (AMANHI project). This system was in place to serve a research project that was on going at the time. Under this system all households in the Shivgarh block were visited bi-monthly by trained CEL staff to identify women with missed menstrual periods. The date of last menstrual period (LMP) was recorded for any women who reported a missed menstrual period, ensuring early identification of pregnancies.

Table 2.1 Major seasonal characteristics in Shivgarh (constructed from field interviews in Shivgarh between May and August 2013)

Season	Rainy (June-September)				Winter (Oct-Feb)					Summer (Mar-May)		
	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
Peak Rainfall		X	X	X								
Peak Temperature	X											X
Staple crop harvest	P_h	R_s			R_h	R_h	W_s			W_h	W_h/P_s	
Peak Agriculture Labor demands	X	X			X	X				X	X	
Peak infectious disease risk		X	X	X								
Diminished food security		X	X	X								

P_s:= pepper sowing; P_h = peppermint harvesting; R_s= rice sowing; R_h = rice harvesting; W_s= wheat sowing; W_h=wheat harvesting

At recruitment (pregnancy visit), a brief questionnaire was administered to women to collect information about pregnancy history and household socioeconomic status. Pregnant women were eligible for inclusion in the study if they had no severe health conditions, and no plans to migrate for more than four months during the study period (n=599). Mother-infants pairs were permanently lost to follow-up if either the mother or infant died (including still-birth and miscarriage) (n=66), if the family permanently migrated from the study area (n=36), or if the mother revoked consent (n=2). Mother-infant pairs were temporarily lost to follow-up if they were not visited within 14 days of the infant's monthly birthday (either due to field constraints, or unavailability of the mother-infant pair for interview) (**Figure 2.3**). Pre-term infants (gestational age less than 37 weeks) are expected to have different patterns of postnatal growth than term infants, and were thus excluded from analyses (n=66) [118]. The sample was intended to represent a near universal sample of healthy pregnant women in their third trimester of pregnancy from these select villages.

2.3 Anthropometric assessment

At each visit, maternal and paternal (if available) and infant anthropometry was collected. Adult anthropometry included height, weight and mid-upper arm circumference (MUAC; mothers only). Infant anthropometry included crown-heel and crown-rump length, weight, and calf, head and mid-upper arm circumferences (MUAC; measured for six month old infants) were collected using standard techniques by trained and standardized enumerators [119].[5] In this study, we sought to detect relatively small changes in infant growth and therefore conducted extensive training, standardization and quality control to minimize measurement error. Enumerators were trained and standardized on anthropometry according to WHO Multi-Center Growth Reference Study (MGRS) protocols at the onset of the study, and then four additional times throughout the data collection period [120]. Any enumerator who did not meet the MGRS levels of measurement precision, or technical error of measurement (TEM), or who showed signs of bias as compared to the expert reference anthropometrist were provided with additional training and practice [120]. The mean and range of TEM values for the study enumerators at three study time points is shown in **Table 2.1**. Enumerators were trained, but not standardized on weight measures, because the measurement error for a digital scale is expected to be negligible relative to other

[5] The anthropometric measures considered in this dissertation are maternal and infant weight and height/length.

sources of error.

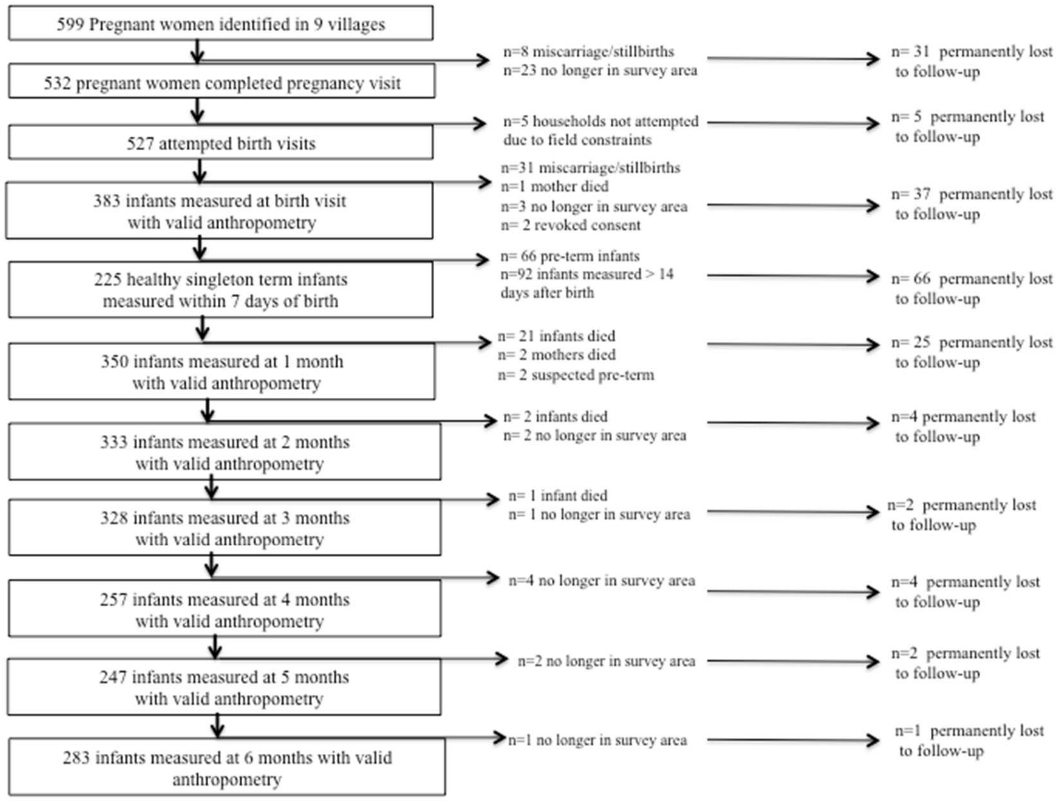


Figure 2.3 Diagram of participants included in the study [6]

[6] Infants who were not permanently lost to follow-up, but not measured at any given visit were temporarily unavailable (e.g. temporary refusal, or mother not at home at time of visit). If not available for visit, and field staff were available, up to three additional visits were attempted. If not reached within 14 days of the infant's scheduled monthly visit the data was lost, but the infant remained available for future visits. Due to field constraints the ability to revisit was often times not possible.

Table 2.2 Mean (Range) Technical Error of Measurement (TEM) values for anthropometry at various training and standardization sessions

Measure	WHO MGRS	July/August 2014	January/February 2015	January/February 2016
Infant Measures				
Crown-heel length[c]	0.33[a] (0.21-0.58)	0.50[b] (0.39-0.64)	0.23[b] (0.12-0.32)	0.25[b] (0.18-0.35)
Crown-rump length	N/A; Used Crown-heel length reference	0.84 (0.48-1.43)	0.47 (0.33-0.62)	0.28 (0.23-0.38)
Calf circumference	N/A; Used child MUAC reference 0.17 (0.15-0.27)	0.19 (0.15-0.21)	0.14 (0.10-0.17)	0.18 (0.14-0.21)
Head circumference	0.12 (0.13-0.29)	0.21 (0.19-0.25)	0.18 (0.15-0.20)	0.17 (0.11-0.31)
Maternal Measures				
Height[cd]	0.28 (0.27-0.30)	0.21 (0.14-0.26)	0.21 (0.14-0.26)	0.21 (0.14-0.29)
Maternal mid-upper-arm circumference (MUAC)	N/A; Used child MUAC reference 0.17 (0.15-0.27)	0.22 (0.17-.30)	0.15 (0.06-0.24)	0.18 (0.11-0.27)

[a] Mean TEM (acceptable range)
[b] Mean TEM (enumerator range) for nine anthropometrists
[c] Measures used in this thesis
[d] TEM values for adult height are not available from MGRS and so reported mean and range for this measure are from the Children's Healthy Living Program [121]

Maternal and paternal heights were measured with the subject standing on a flat surface using a portable stadiometer to the nearest 1 mm (Seca Corporation, Hamburg, Germany, model 213). Infant crown-heel and crown-rump length were measured on a flat surface with a portable infantometer to the nearest 1 mm (Schorr Industries, Glen Burney, MD). Maternal MUAC and infant circumferences were measured using a non-stretchable Teflon measuring tape to the nearest 1 mm (Seca Corporation, Hamburg, Germany, model 212). Weight was measured on a flat surface with minimal clothing with an electronic mother-infant scale to the nearest 50 g (Seca Corporation, Hamburg, Germany, model 874). Scales were calibrated daily with standardized weights [119].

Our goal was to weigh infants wearing little or no clothing. This was not always feasible, however, due to concerns about measuring unclothed infants, especially shortly after birth, and in harsh weather conditions (most anthropometry was measured in patio areas outside the home). In an attempt to standardize what the infant wore during measurement, standard size infant blankets of known weight were distributed to each mother-infant pair enrolled in the study. If the infant could not be weighed in little or no clothing (e.g. mother refusal, extremely cold temperature), they were undressed and then wrapped in the standard blanket before weighing. Enumerators then recorded whether the standard blanket and other individual clothing items (each item listed in the form) were worn during measurement. At a later time, field staff collected weights for standard versions of these clothing items for infants of different ages from nearby non-study villages in the Shivgarh block. Clothing weights were measured to the nearest 0.5 g using a locally procured digital kitchen scale. The weights of all individual clothing items worn by a child were summed and then subtracted from the recorded weight of the child. At each visit, two measurers independently collected a complete set of anthropometric measures (except for weight) and then compared results. If upon comparison, the difference between the two enumerator's results for any measure was outside of the MGRS defined maximum allowable difference, each measurer independently repeated the measure and compared results [120]. This procedure was repeated up to a maximum of three times to reduce inter-observer measurement error. All available measures for an infant from a single measurement session were averaged for use in analyses, unless a measure or re-measure was considered biologically implausible during data cleaning.

2.4 Estimation of gestational age

Gestational age of the infant at time of birth was calculated retrospectively as the difference between infant date of birth and maternal recall during early pregnancy of the date at the beginning of her last menstrual period (LMP). Because LMP is prone to estimate gestational age with error, we assessed the plausibility of gestational age values in several ways. First, univariate linear regression models of gestational age with various measures of size at birth (crown-heel length, crown-rump length, weight and head circumference) were used to identify infants with gestational age values that were inconsistent with body size. Residuals from any of these models that were ± 3 standard deviations from the mean were classified as outliers and individual values were set to missing (n=2). Next, predicted values of gestational age based on head circumference measured at birth were generated and compared to calculated values of gestational age. Head circumference was chosen as a predictor because it is related to gestational age, but was not used as a dependent variable in any of the present analyses. Infants with a calculated gestational age greater than 43 weeks, or for whom the calculated and predicted values of gestational age differed by ± 5 weeks, were considered errors (likely the result of error in recall or recording of LMP) and individual values were also set to missing (n=27 and n=12, respectively) [122].

2.5 Data collection and management

All data from this study were recorded on tablet computers and later downloaded to Excel spreadsheets which were uploaded to Stata version 13, the program used for all data cleaning and analyses [123]. For questionnaire data, completion of the questionnaire and plausibility of responses were thoroughly examined for all data. For example, in the morbidity questionnaire, if a mother was asked whether or not she had symptoms of fever in the past 30 days, and she responded no, then a response should not have been recorded for the subsequent question regarding symptoms in the past seven days. If a response was recorded, values for both questions were set to missing because we were unable to determine which response was an error. For the number of days of symptoms in the past seven days, the plausible range of responses was 0-7 days. Values outside of this range (likely the result of recording errors) were determined implausible and individual values were set to missing. A similar systematic data cleaning approach was followed for all questionnaire data.

Anthropometric data were scrutinized within and between visits for biologically implausible measures in weight and length (likely due to measurement and recording errors). For each anthropometric measure, the residuals of simple univariate regression models (e.g. weight vs. crown-heel length, weight vs. head circumference, weight vs. calf circumference etc.) were first examined to assess the internal consistency of measures within a child. Residuals ± 3 SD from the mean were considered as an indication of lack of consistency between body measures within the same child. Inconsistent measures were visually examined in two-way scatterplots to determine biological plausibility. To identify extreme values, raw attained weight and length values were converted to age and sex specific Z-scores based on the MGRS growth standard. Outlier Z-score values were defined according to WHO recommendations as per the following criteria: length-for-age Z-scores (LAZ) less than -6 or greater than 6; weight-for-age Z-scores (WAZ) less than -6 or greater than 5; weight-for-height Z-scores (WLZ) less than -5 or greater than 5 [124]. Outlier Z-scores or otherwise implausible values were excluded from the analyses (n=9 length values and n=12 weight values). Although WHO Z-scores could not be generated for infants with length measures less than 45.0 cm, these measures were considered biologically plausible in this setting, and were consistent with small size for other measures within the same child (n=16; range 41.5-45.0 cm). These values were thus included in the analyses.

For additional scrutiny of the growth trajectory data, measures of individual infant size were plotted and visually examined by infant age. No infant measures were found to exhibit biologically implausible patterns of postnatal growth (e.g. extreme crossing of the MGRS centiles). Two additional infants, however, were suspected of being preterm based on their postnatal growth patterns (born very small followed by higher than expected growth velocity between birth and one month), and were thus excluded from additional analyses of longitudinal growth [118]. For crown-heel and crown rump length, observed decreases of greater than 0.7 cm between any two visits (level of acceptable measurement error between visits in the MGRS study) within a child were considered possible errors and were further scrutinized. Individual length values determined to be biologically implausible were set to missing (n=11) [120]. More in depth descriptions of the data are described in Chapters 3-5.

2.6 Statistical methods

The sample size for the present research was based on the outcome of length velocity in two-month growth increments. The minimum difference between two groups is the smallest biologically important difference in growth rate, and based on previously reported literature, a 0.5 standard deviation difference (0.45 cm/2 month increment from 4-6 months of age or 0.225 cm/month) from the MGRS growth standard median was deemed biologically significant [65, 98, 125]. To perform a test of two independent sample means with an effect size of 0.45 cm, an alpha of 0.05 and power of 90%, we estimated that 17 infants were needed per month. Assuming a design effect of 1.15 to account for the clustering of villages, and a 30% loss to follow-up, we planned to recruit a sample of 25 infants per month in order to detect the desired difference in length velocity. Similar calculations confirmed that this sample size was adequate to detect a 100 g/ 2 month increment difference in weight velocity. All sample size calculations were performed using SAS version 9.2 (SAS Institute, Cary, NC, USA)

Chapter 3
Aim 1: Variation in early neonatal size by month of conception in rural Uttar Pradesh, India

Madan EM, Haas JD, Frongillo EA, Rasmussen KM, Kumar V, Kumar A, Menon P

3.1. Abstract

India has one of the world's largest burdens of small size at birth, an important predictor of short and long-term negative health and economic consequences. In tropical and sub-tropical regions of developing countries, recurrent seasonal stress may be an important determinant of small size at birth. The aim of this study was to examine whether there was an association between monthly variation in conception and early neonatal size (weight and length) in an agrarian population in north India. Pregnant women from nine purposefully selected villages in Uttar Pradesh, India were recruited between July 2014 and September 2015 to participate in a longitudinal study of infant growth. We conducted exploratory regression analyses to examine whether month of conception was associated with variation in early neonatal size (measured within seven days of birth) after accounting for important time-invariant maternal and infant characteristics.

Regression analyses suggest that infants conceived between July and September 2014 had early neonatal weights that were significantly lower (approximately 208 g) than the overall sample mean weight. Infants conceived between April and June 2014 had marginally significantly lower early neonatal recumbent lengths (approximately 0.6 cm) compared to the overall sample mean length. These differences are likely a reflection of health or nutritional insults that

occurred during different stages of pregnancy. A better understanding of possible monthly or seasonal insults to fetal growth can inform programs and policy to ameliorate fetal growth restriction at birth in rural agrarian populations.

3.2 Introduction

Small size at birth is an important predictor of poor postnatal growth and development and both short and long-term negative health and economic consequences [18, 126-128]. Previous research on the determinants of small size at birth has highlighted the importance of nutrition and socio-demographic factors including low pre-pregnancy maternal weight, short maternal stature, young maternal age, primiparity, low maternal education, low socio-economic status, and heavy work during pregnancy [30, 129-132].

In tropical and sub-tropical regions of developing countries, seasonal stress is also a risk factor for reduced size at birth. This is because monthly variations in climate drive the agricultural cycle and, thus, factors such as the demands for labor and availability of locally produced food [73]. Monthly fluctuations in the incidence of infectious disease have also been reported [102, 107, 108]. Month of birth, which can be used as a proxy for the time of gestation, has been associated with size at birth in various African and South Asian countries [90]. Reductions in birth size that occur during certain months of the year are largely attributed to a deterioration in maternal nutritional status during critical stages of gestation resulting from a convergence of risk factors such as food shortages, high agricultural labor demands, and high risk for infectious disease [39, 73, 90, 95].

In India, nearly 50% of infants are born small-for-gestational age (SGA), an indicator of poor intrauterine growth, and nearly 50% of children under five years of age suffer from linear growth faltering (stunting), much of which is already present at birth [17]. Nearly 70% of the Indian population continues to reside in rural areas and remains largely dependent on agriculture for their livelihoods [70, 133]. Consequently, a large proportion of the population is susceptible to risk factors for poor health and nutritional status that vary according to annual climatic and agricultural cycles. Monthly differences in size at birth are poorly understood in rural India, and the available literature focuses largely on rain-fed agricultural systems, where typically only one crop is grown per year [39, 73, 93]. The aim of this paper was to examine whether there is variation in early neonatal size (weight and length) that occurs throughout the year in a rural agrarian population in India where access to irrigation is prevalent. An understanding of the monthly patterns in size at birth can be used to inform programs and interventions targeted to improve fetal growth, assessed as size at birth.

3.3 Methods

3.3.1 Subjects and sample

This study was conducted in nine purposefully selected villages of the Shivgarh block in the Rae Bareli district in Uttar Pradesh, India. The nine villages were purposefully selected by the Community Empowerment Lab (CEL) (local collaborating non-governmental organization) field managers, with in-depth knowledge of the local area, to be representative of the socio-economic and agricultural variability of the Shivgarh block, and also to have a sufficient number of births per month to meet sample size requirements.

Uttar Pradesh is the largest state in India by population and performs poorly on indicators of child health and nutrition. The Rae Bareli district, located approximately 70 km from the capital city of Lucknow, has prevalence estimates of child (less than five years of age) stunting, wasting and underweight of 36.1%, 32% and 42.2%, respectively [6]. Seasonal patterns in Shivgarh are described in detail in Chapter 2. In brief, the climate in Shivgarh is subtropical, and has three main seasons: summer (April-June), monsoon (July-September) and winter (October-March). The primary livelihoods in Shivgarh are semi-subsistence farming and agricultural labor. The staple crops are rice and wheat, and peppermint is grown as a cash crop. Most farmers have access to irrigation via canals and tube wells and report that periods of peak labor demands correspond to the rice sowing (monsoon season), rice harvest (October-November) and wheat harvest periods (March-April). Rural agriculturalists in Shivgarh report that the period from July to September is a risk period for low food availability if the supply of wheat begins to run low while the rice crop is still in the field.

From July 2014 to September 2015, all 599 healthy pregnant women in the 32nd week of pregnancy or later, residing in the nine selected villages in the Shivgarh block were invited to participate in a longitudinal study of infant growth. To identify pregnancies, households in the study area were visited bi-monthly by surveillance staff and women of reproductive age were asked to recall the date of their last menstrual period (LMP). Pregnant women, who accepted participation and signed informed consent were enrolled in the study and scheduled to be visited a total of eight times: at pregnancy (enrollment; during the third trimester), at birth, monthly from 1-6 months of infant age and then again at nine and 12 months of infant age (**Figure 2.2**). A notification system was established for births with the goal of collecting infant anthropometry as close to birth as possible, ideally within the first 72 hours. As a result of logistical challenges, however, this proved infeasible. Three hundred seventeen full term newborn infants were measured within 14 days of birth. Ten percent were measured within one day, 64% were measured within three days, 71% were measured within seven days, and 97.5% of infants were measured within 14 days of birth.

At each visit, a team of trained and standardized enumerators, working in pairs, administered structured questionnaires to pregnant women and the head of the household or other knowledgeable household member. Detailed information on maternal, infant and socio-demographic characteristics were collected, and maternal and infant measurements were taken in duplicate by two independent anthropometrists during the last trimester of pregnancy (mean time of measurement at 34.0 ± 2.1wk of pregnancy). Maternal height was measured with the subject standing on a flat surface using a portable stadiometer to the nearest mm (Seca Corporation, Hamburg, Germany, model 213). Weight was measured on a flat surface with minimal clothing with an electronic mother-baby scale to the nearest 50 g (Seca Corporation, Hamburg, Germany, model 874). Scales were calibrated on a daily basis using standard techniques [119]. Maternal mid-upper arm circumference (MUAC) was measured using a non-stretchable Teflon measuring tape to the nearest 1 mm (Seca Corporation, Hamburg, Germany, model 212). Infant weight was taken with the electronic mother-infant scale previously described, and crown-heel length was measured on a flat surface with a portable infantometer to the nearest 1 mm (Schorr Industries, Glen Burney, MD). Enumerators were trained and standardized according to the WHO Multicentre Growth Reference Study (MGRS) protocols at the onset of the study, and then periodically throughout data collection (mean technical error of measurement (TEM) (range) for crown-heel length = 0.33 (0.12-0.64) cm; TEM for maternal height=0.21 (0.14-0.26) cm) [120].

The data presented here are the early neonatal (0-7 days) anthropometry for singleton, full term (greater than or equal to 37 weeks) infants enrolled in a longitudinal study of infant growth (n=225) (**Figure 3.1**). Data for infants measured more than seven days after birth were excluded from analyses due to concerns that measures taken so late after birth could add unwanted variation to analyses and potentially dilute the effect of prenatal variables of interest. The International Food Policy Research Institute (IFPRI) and the Community Empowerment Lab (CEL) ethical review boards provided ethical approval for this study, following guidelines for the Helsinki Declaration of 1975 as revised in 1983 [134].

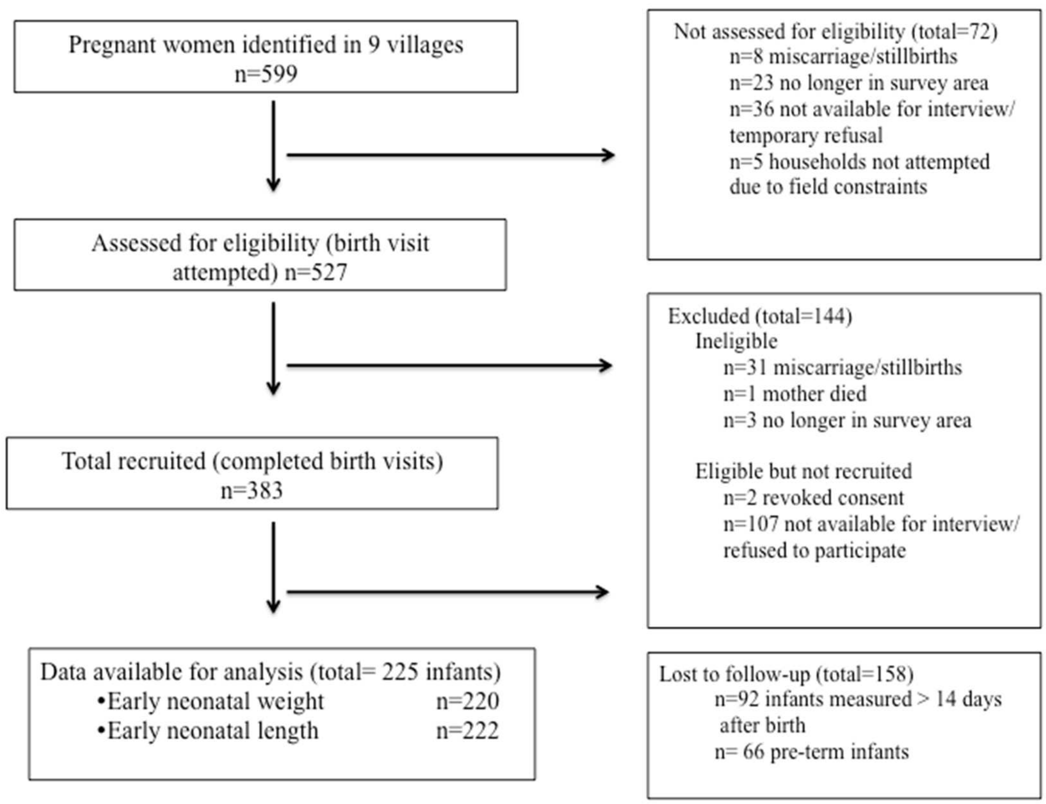


Figure 3.1: Study profile

3.3.2 Measurements

We conducted exploratory analyses to examine whether month of conception (exposure), calculated as the difference between infant date of birth and gestational age, was associated with variation in the outcomes of early neonatal weights and lengths after accounting for important time-invariant maternal and infant characteristics (mean time of first maternal interview and measurement at 34.0 ± 2.1 weeks of pregnancy) **(Figure 1.3).** Because SGA has greater public health implications than early neonatal absolute weight (e.g. greater risk of morbidity and mortality), we also examined whether maternal characteristics and month of conception were associated with risk of SGA in secondary analyses. Dependent variables considered in the analyses were early neonatal weight and length, and SGA. Weight and length were considered as continuous variables and SGA was considered as a binary categorical variable. Where duplicate anthropometric measures were recorded, values were averaged for use in analyses. Early neonatal weights were corrected for clothing by summing the weight of recorded clothing items (based on weights of locally available standard clothing items), and then subtracting this sum from the recorded weight of the child. For data cleaning, raw values for infant length and weight were converted to Z-scores based on the MGRS growth standard [135]. Outlier Z-score values were defined according to the following criteria: length-for-age Z-scores (LAZ) less than -6 or greater than 6; weight-for-age Z-scores (WAZ) less than -6 or greater than 5; weight-for-height Z-scores (WHZ) less than -5 or greater than 5 [124, 135]. Outlier Z-scores and associated raw data values were excluded from the analyses (n=3 length values and n=9 weight values). Infants were categorized as SGA if their weight was below the 10th centile of newborn weights based on the INTERGROWTH-21st growth reference [122]. Ponderal index (PI) of infants was calculated according to the equation: infant weight (g) *100/ (crown-heel length [cm])^3. SGA infants were classified as either low PI (suggestive of acute growth restriction) or high PI (suggestive of chronic growth restriction), if they had a PI of less than 2.25 or greater than or equal to 2.25, respectively [136].

We examined biological and socio-demographic variables that we hypothesized to be associated with early neonatal size. Risk factors were organized in three categories: infant, maternal biological, and socio-demographic. Infant variables considered in the analyses were sex, gestational age, and postnatal age at time of measurement. Gestational age of the infant at the time of birth was calculated retrospectively as the difference between infant date of birth and maternal recall during early pregnancy of her date at the beginning of LMP. Because LMP is prone to estimate gestational age with error, the plausibility of gestational age values were assessed and individual values determined to be biologically implausible were set to missing (n=41). Date of LMP for these individuals was also set to missing. Maternal biological variables were height and parity. Height was considered as a continuous variable and parity was classified as primiparous (1) and multiparous (greater than one) for current and previous pregnancies (born live or stillborn).

Socio-demographic factors included household food insecurity, socio-economic status, maternal education, village, and month of conception. Household food insecurity scores were calculated and households were classified into four food insecurity categories according to FANTA guidelines [137]. Few women (n=3) fell into the most severe categories of food insecurity and so food security scores were collapsed into two categories: food-secure and food-insecure. Socio-economic status (SES) of the household was derived from household assets (e.g. television, refrigerator, motorcycle, tractor, etc.) and from household construction materials (e.g., roof, floor and walls). Principal components analysis (PCA) was used to compute a household SES score, which was then ordered using tertiles (e.g. the first tertile represented the lowest SES group, etc.) [138]. Maternal education was recorded in one of four categories: never went to school, started school but did not finish grade 1, completed 12th standard, and completed bachelors or technical school. Because the categories of education were imprecise, we were only able to accurately distinguish women with no education compared to those who any education. Therefore, maternal education was collapsed into a dichotomous variable accordingly.

In exploratory analyses, months of conception were first considered in disaggregated form. In as much as few infants were conceived in individual months, months were combined into one two-month period (November-December 2013) and four three-month periods (January-March 2014; April-June 2014; July-September 2014; October- December 2014). These periods were chosen for two reasons. First it was assumed that consecutive months were likely to have similarities in underlying climate and agricultural characteristics. Second, this aggregation of months provided more statistical power for regression analyses as compared to other aggregation options (e.g. two month groupings, or grouping of the last two months rather than the first two months of conception).

3.4 Statistical methods

3.4.1 Sample size

Previously published research studies conducted in South Asia have shown birthweight and birth-length differences throughout the year ranging from approximately 80 g to 145 g and 0.3 cm to 1.5 cm, respectively [39, 93, 125]. We estimated the sample size for the present chapter to enable us to detect a 100 g difference between monthly mean early neonatal weights and the overall sample mean weight at 80% power, a significance level of 5%, a design effect of 1.15 (to account for clustering of villages). Based on these assumptions, we estimated that approximately 230 infants were needed (approximately 17 infants/month). Similar calculations confirmed that this sample size would be adequate to detect a 0.5 cm difference between mean early neonatal lengths and the overall sample mean length.

3.4.2 Statistical analyses

To examine the association between months of conception and early neonatal size, multivariable regression analyses were conducted separately for early neonatal weights and lengths and SGA. Missing data for independent variables was assumed to be missing at random (MAR), and were thus handled using a structural equation modeling procedure that implemented full information maximum likelihood [139]. For secondary analyses of the association between months of conception and SGA, however, only data for complete cases were used. Adjustments were made for variables that could potentially confound the relationship between three-month periods of conception and early neonatal size. Potential confounding was considered for any covariate with a p-value < 0.2.

To account for potentially nonlinear physiological weight change in the infant during the first seven days of life, a quadratic infant age term and a categorical age term (0-2, 3-5 and 6-7 days) were explored in sensitivity analyses of early neonatal weight as the dependent variable. A nonlinear relationship was not observed between either of these age terms and early neonatal weight, and thus only a linear age term was included in the final model. In multivariable regression models, we observed evidence of collinearity between village and SES. We chose to include only village in final models because village was believed to better capture observed SES differences as well as other potentially unobserved characteristics between villages. We also tested an interaction between gestational age and three-month conception periods because it was possible that the period of conception modified the relationship between gestational and early neonatal size, but no significant interaction was observed. Stata's post-estimation procedure, *lincom*, was used to estimate marginal means in each three-month conception period at the mean value of all model covariates. The post-estimation procedure analyzed the stored results of the SEM model. The *lincom* procedure was then used to compare marginal means to the overall sample mean for models of early neonatal weight and length, separately, and to the overall sample odds for models of SGA. Marginal means were estimated because we were interested in the mean values of early neonatal size adjusted for other model covariates. We compared estimated marginal means of early neonatal size in each three-month conception period to the overall sample mean because this difference was thought to be a more meaningful reflection of differences throughout the year as compared to between month comparisons. Because food insecurity was only assessed at late pregnancy but could vary throughout pregnancy it was considered as a potentially time-variant characteristic. Therefore, we compared model coefficients for models including and excluding the food insecurity variable to examine whether there was evidence that food insecurity acted as a mediator of the relationship between three-month period of conception and early neonatal size. All analyses were conducted using Stata version 13 (StataCorps, TX). Statistical significance was defined as $p<0.05$.

3.5 Results

Study participants were relatively young (mean ± SD, 25.5 ± 5.0 y; range 18-53 y), and nearly one-third of the study cohort was composed of primiparous mothers. Primary occupation in agriculture or day labor was reported by approximately 79% of heads of household. A greater proportion of infants were classified as SGA than low birth weight (LBW) (approximately 54% and 34%, respectively) **(Table 3.1).**

The maximum difference in mean early neonatal weights and lengths between any two months of conception was 375 g (November 2013 and September 2014) and 2.9 cm (November 2013 and March 2014), respectively (**Figure 3.2; Figure 3.3:**

Appendix B). There were large differences in the number of infants conceived each month and our sample likely does not represent a universal sample of births in these nine study villages (range 4-30 infants/per month). The greatest difference in mean early neonatal weights and lengths between any two three-month conception periods was 326 g (November-December 2014 and July-September 2014) and 1.5 cm (November-December 2014 and April-June 2014), respectively. The lowest percentage of SGA (40%) infants occurred in the October-December 2014 period, when the mean early neonatal length was relatively high (**Table 3.2**). The highest percentage of low PI infants occurred in the July-September 2014 period, the same period when the mean early neonatal weight was the lowest

Table 3.1: Characteristics of women, infants and households in Shivgarh (n=225)

Characteristic	Mean ± SD	N (%)
Infant characteristics		
Early neonatal weight, g (n=220)	2699 ± 492	---
Small for gestational age, <10th centile of Intergrowth-21st reference (n=178)	---	93 (53.8)
Low birth weight, <2500 g	---	75 (34.1)
Early neonatal length, cm (n=222)	47.9 ± 2.2	---
Low birth-length, <10th centile of Intergrowth-21st reference	---	65 (29.3)
Gestational age, wk (n=178)	39.6 ± 1.4	---
Infant postnatal age, d	3.0 ± 2.1	---
Female		113 (50.2)
Maternal Biological Characteristics		
Height, cm (n=202)	149.9 ± 5.4	---
Attained Weight During 3rd trimester, kg (n=178)	49.6 ± 7.5	---
Mid-upper arm circumference, cm (n=222)	23.2 ± 2.2	---
Maternal age, y (n=221)	25.5 ± 5.0	---
Parity (n=200)	2.8 ± 2.0	---
Primiparous		56 (28.0)
Socio-demographic characteristics		
Marital Status (n=221)		
Married	---	220 (99.6)
Maternal Education (n=221)		
Never went to school	---	75 (33.9)
Went to any school	---	146 (66.1)
Socio-economic status (n=208)	---	
Lower class	---	70 (33.7)
Middle class	---	67 (32.2)
Upper class	---	71 (34.1)
Land (n=218)		
Owns land	---	141 (64.7)
Small holder farmers (<2.0 hectares)	---	209 (95.9)
Household Food Insecurity Score (n=218)	1.2 ± 2.2	---
Food insecure		74 (33.9)
Village (n=225)		
Village 1	---	30 (13.3)
Village 2	---	32 (14.2)
Village 3	---	22 (9.8)
Village 4	---	37 (16.4)
Village 5	---	30 (13.3)
Village 6	---	5 (2.2)
Village 7	---	14 (6.2)
Village 8	---	34 (15.1)
Village 9	---	21 (9.3)

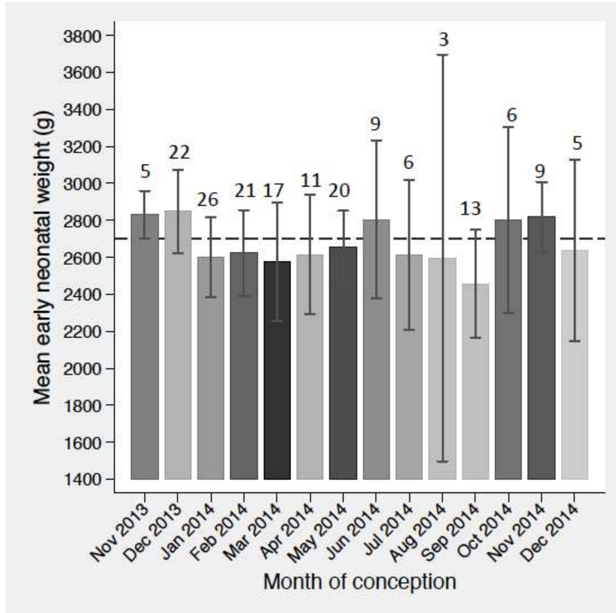


Figure 3.2 Unadjusted birthweights by month of conception (mean ± SE). The dashed horizontal line represents the overall sample mean of 2699 g. Numbers at the top of each bar represents sample size

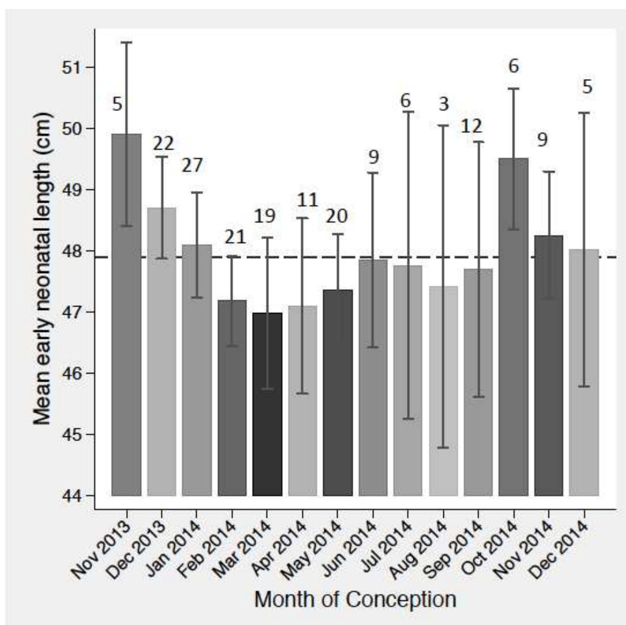


Figure 3.3 Unadjusted birth-lengths by month of conception (mean ± SE). The dashed horizontal line represents the overall sample mean of 47.9 cm. Numbers at the top of each bar represents sample size

Table 3.2 Unadjusted early neonatal weights and lengths, number of small-for-gestational age (SGA), and number of low ponderal index (PI) by three-month periods of conception

3-Month Conception Periods	Weight[a]	Length[a]	Proportion of SGA births (%)	Proportion of low PI births (% of all SGA births)
Nov-Dec 2013	2845 ± 457 (n=27)	48.9 ± 1.8 (n=27)	14 (51.9)	6 (46.2)
Jan-Mar 2014	2601 ± 541 (n=64)	47.5 ± 2.2 (n=67)	38 (59.4)	15 (39.5)
Apr-Jun 2014	2676 ± 464 (n=40)	47.4 ± 2.0 (n=40)	21 (52.5)	8 (38.1)
Jul-Sep 2014	2519 ± 441 (n=22)	47.7 ± 2.7 (n=21)	12 (54.6)	6 (54.6)
Oct- Dec 2014	2768 ± 353 (n=20)	48.6 ± 1.5 (n=20)	8 (40.0)	3 (37.5)

[a] Mean ± SD

Based on multivariable regression analyses, unit differences in gestational age (wk) and maternal height (cm) both had significant positive associations with early neonatal weight ($p < 0.05$), while primiparity, mother having any education, mother being food insecure during late pregnancy, and female infant sex all had significant negative associations ($p<0.05$) (**Table 3.3**). Infant postnatal age at time of measurement (0-7 days) was not significantly associated with early neonatal weight ($p=0.93$). After controlling for important time-invariant maternal, infant and socio-demographic characteristics, early neonatal weights were lower in all three-month conception periods, relative to the November-December 2013 reference period. Only the mean early neonatal weights in the July-September 2014 conception period, however, were significantly lower (-313.7 ± 122.3 g; $p=0.010$) than the reference period. Mean early neonatal weights in the July-September 2014 conception period were 208 g lower ($p=0.020$) than the overall sample mean, while other three-month conception periods were not significantly different from the overall mean weight (**Table 3.4**). Whether the food insecurity variable was included or excluded from models revealed only minor changes in model parameters and no change in model inference. Food insecurity therefore did not appear to act as a mediator between three-month period of conception and early neonatal weight.

Single unit differences in infant postnatal age at time of measurement, gestational age and maternal height had significant positive associations ($p< 0.05$) with early neonatal length, while primiparity, female sex, and mother being food insecure during late pregnancy all has significant negative associations ($p<0.05$) (**Table 3.5**). The association between early neonatal length and mother having any education was negative, but not statistically significant ($p=0.122$). Relative to the November-December 2013 reference period, mean early neonatal lengths were significantly lower in January-March 2014 ($p=0.018$), April-June 2014 ($p=0.002$) and July-September 2014 ($p=0.008$) (**Table 3.5**). After controlling for significant covariates and computing the post-estimation marginal means, only the mean lengths in the April-June 2014 period were marginally significantly lower than the overall sample mean ($p=0.084$), while infants conceived during November and December 2013 were significantly larger than the overall sample mean ($p=0.008$) (**Table 3.6).** Whether the food insecurity variable was included or excluded from models resulted in negligible changes in model parameters and no change in model inference. Food insecurity therefore did not appear to act as a mediator between three-month period of conception and early neonatal length.

Table 3.3 Association of maternal[a] and infant[b] variables and three-month periods of conception with early neonatal weights (g) using structural equation modeling[c]

Independent Variables	Model 1[d] (n=220)	Model 2 [d] (n=220)	Model 3 [d] (n=220)	Model 4 [d] (n=220)
Infant postnatal age, d	---	1.2 ± 15.8 p=0.94	-3.9 ± 14.3 p=0.79	-1.3 ± 14.2 p=0.93
Gestational age, wk	---	57.4 ± 25.2 p=0.023	63.9 ± 22.4 p=0.004	62.8 ± 22.1 p=0.004
Male	---	Ref	Ref	Ref
Female	---	-202.7 ± 64.1 p=0.002	-206.1 ± 58.2 p<0.001	-235.5 ± 58.3 p<0.001
Maternal height, cm	---	---	30.3± 5.7 p<0.001	28.9 ± 5.7 p<0.001
Multiparous	---	---	Ref	Ref
Primiparous	---	---	-283.0 ± 70.5 p<0.001	-307.8 ± 69.8 p<0.001
No education	---	---	Ref	Ref
Any education	---	---	-150.7± 66.3 p=0.023	-173.2 ± 65.5 p=0.008
Food Secure	---	---	---	Ref
Food Insecure	---	---	---	-181.8 ± 66.0 p=0.006
Conceived Nov-Dec 2013	Ref	---	Ref	Ref
Conceived Jan-Mar 2014	-224.6 ± 109.8 p=0.041	-183.7 ± 107.7 p=0.088	-141.4 ± 96.9 p=0.14	-147.4 ± 95.9 p=0.12
Conceived Apr-Jun 2014	-136.6 ± 120.7 p=0.26	-118.2 ± 117.7 p=0.32	-71.1 ± 104.6 p=0.50	-56.4 ± 103.8 p=0.59
Conceived Jul-Sep 2014	-361.1 ± 140.8 p=0.010	-337.5 ± 139.0 p=0.015	-289.3 ± 123.8 p=0.019	-313.7 ± 122.3 p=0.010
Conceived Oct-Dec 2014	-24.1 ± 143.4 p=0.87	-32.7 ± 140.3 p=0.816	-13.6 ± 126.1 p=0.91	-20.6 ± 125.1 p=0.87
R^2	.09	0.15	0.33	0.35

[a] Maternal variables include height, parity and education
[b] Infant variables include postnatal age, gestational age and sex
[c] All models control for village as a fixed effect
[d] Coefficient ± SE

Table 3.4 Marginal means of early neonatal weights (g) for three-month conception periods estimated at the mean value of all covariates. P-values were derived from the post-estimation comparison of the mean early neonatal length in each three-month conception period to the overall sample mean early neonatal weight (g)

Three-month conception periods	Early neonatal weight marginal means (g)[a] *Model 3* *excluding food insecurity*	Early neonatal weight marginal means (g)[a] *Model 4* *including food insecurity*
Conceived Nov–Dec 2013 (n=27)	2801 ± 79 p=0.20	2804 ± 79 p= 0.18
Conceived Jan-Mar 2014 (n=64)	2659 ± 51 p=0.43	2657 ± 50 p= 0.40
Conceived Apr-Jun 2014 (n=40)	2729 ± 65 p=0.64	2748 ± 64 p=0.44
Conceived Jul-Sep 2014 (n=22)	2511 ± 91 p=0.039	2491 ± 90 p=0.020
Conceived Oct-Dec2014 (n=20)	2787 ± 96 p=0.36	2784 ± 96 p=0.37
Overall sample mean	2699 ± 33	2699 ± 33

[a] Mean ± SE

Table 3.5 Association of maternal[a] and infant[b] variables and three-month periods of conception with early neonatal lengths (cm) using structural equation modeling[c]

Independent Variables	Model 1[days] (n=222)	Model 2 [d] (n=222)	Model 3 [d] (n=222)	Model 4 [d] (n=222)
Infant post-natal age, d	---	0.18 ± 0.07 p=0.010	0.16 ± 0.07 p= 0.014	0.17 ± 0.06 p=0.007
Gestational Age, wk	---	0.20 ± 0.11 p= 0.072	0.24 ± 0.10 p=0.020	0.24 ± 0.10 p=0.022
Male Sex	---	Ref	Ref	Ref
Female sex	---	-0.59 ± 0.28 p=0.037	-0.59 ± 0.27 p=0.028	-0.74 ± 0.27 p=0.006
Maternal height, cm	---	---	0. 12 ± 0.026 p<0.001	0.12 ± 0.03 p<0.001
Multiparous	---	---	Ref	Ref
Primiparous	---	---	-1.05 ± 0.32 p=0.001	-1.17 ± 0.31 p<0.001
No education	---	---	Ref	Ref
Any education	---	---	-0.34 ± 0.30 p=0.26	-0.45 ± 0.29 p=0.122
Food Secure	---	---	---	Ref
Food insecure	---	---	---	-0.88 ± 0 .30 p=0.004
Conceived Nov–Dec 2013	Ref	Ref	Ref	Ref
Conceived Jan-Mar 2014	-1.48 ± 0.49 p=0.002	-1.29 ± 0.48 p=0.007	-1.04 ± 0.45 p=0.022	-1.06 ± 0.45 p=0.018
Conceived Apr-Jun 2014	-1.75 ± 0.53 p=0.001	-1.82 ± 0.52 p=0.001	-1.58 ± 0.49 p=0.001	-1.50 ± 0.48 p= 0.002
Conceived Jul-Sep 2014	-1.52 ± 0.64 p=0.018	-1.61 ± 0.64 p=0.011	-1.43 ± 0.59 p=0.015	-1.53 ± 0.58 p=0.008
Conceived Oct-Dec 2014	-0.35 ± 0.65 p=0.60	-0.58 ± 0.64 p=0.37	-0.52 ± 0.60 p=0.38	-0.53 ± 0.59 p=0.370
R^2	0.10	0.16	0.28	0.31

[a] Maternal variables include height, parity and education
[b] Infant variables include postnatal age, gestational age and sex
[c] All models control for village as a fixed effect
[d] Coefficient ± SE

Table 3.6 Marginal means of early neonatal lengths (cm) for three-month conception periods estimated at the mean value of all covariates. P-values were derived from the post-estimation comparison of the mean early neonatal length in each three-month conception period to the overall sample mean early neonatal length (cm)

Three-month conception periods	Early neonatal length marginal means (cm) [a] *Model 3 excluding food insecurity*	Early neonatal length marginal means (cm) [a] *Model 4 including food insecurity*
Conceived Nov–Dec 2013 (n=27)	48.9 ± 0.4 p=0.009	48.9 ± 0.4 p= 0.008
Conceived Jan-Mar 2014 (n=64)	47.9 ± 0.2 p=0.77	47.8 ± 0.2 p=0.72
Conceived Apr-Jun 2014 (n=40)	47.3 ± 0 .3 p=0.044	47.4 ± 0.3 p=0.084
Conceived Jul-Sep 2014 (n=22)	47.5 ± 0.4 p=0.29	47.4 ± 0.4 p=0.195
Conceived Oct-Dec 2014 (n=20)	48.4 ± 0.5 p=0.32	48.4 ± 0.4 p=0.32
Overall Sample Mean	47.9 ± 0.1	47.9 ± 0.1

[a] Mean ± SE

Single unit differences in gestational age, mothers with any education, primiparous mothers, and food insecure mothers were associated with a significant increase in the odds of being born SGA in secondary logistic regression analyses ($p<0.05$; $p=0.053$ for food insecurity variable). The odds of being born SGA were significantly lower (OR=0.91) for each cm difference in maternal height ($p<0.05$). The odds of being born SGA were not significantly different in any of the three-month conception periods as compared to the overall sample odds (**Table 3.7)**. The post-estimation comparison for the SGA model revealed that in the July-September 2014 period, the period when early neonatal weights were the lowest, the odds of being born SGA were higher than the overall sample odds. This difference, however, was not statistically significant ($p=0.38$).

Table 3.7 Association of maternal[a] and infant[b] variables and three-month periods of conception with small-for-gestational age using logistic regression[c]

Independent Variables	Model 1 [d] (n=171)	Model 2 [d] (n=171)	Model 3 [d] (n=152)	Model 4 [d] (n=152)
Infant postnatal age, d	---	0.95 (0.81,1.12) p=0.55	1.01 (0.83, 1.23) p=0.909	1.06 (0.85, 1.32) p=0.63
Gestational Age, wk	---	1.46 (1.14, 1.88) p=0.003	1.47 (1.11, 1.95) p=0.008	1.48 (1.10, 1.99) p=0.010
Maternal height, cm	---	---	0.92 (0.85, 0.99) p=0.028	0.91 (0.83, 0.99) p=0.025
Multiparous	---	---	Ref	Ref
Primiparous	---	---	3.29 (1.31, 8.30) p=0.012	4.80 (1.73,13.32) p=0.003
No education	---	---	Ref	Ref
Any education	---	---	2.29 (0.91, 5.74) p=0.078	2.85 (1.04, 7.81) p=0.042
Food Secure	---	---	---	Ref
Food Insecure	---	---	---	2.51 (0.99, 6.38) p=0.053
Conceived Nov-Dec 2013	Ref	Ref	Ref	Ref
Conceived Jan-Mar 2014	1.24 (0.48, 3.18) p=0.66	1.63 (0.60, 4.38) p=0.34	1.30 (0.41, 4.16) p=0.65	0.92 (0.26, 3.26) p=0.90
Conceived Apr-Jun 2014	0.99 (0.35, 2.77) p=0.98	1.09(0.37, 3.16) p=0.88	0.91 (0.26,0.13) p=0.88	0.59 (0.15,2.38) p=0.46
Conceived Jul-Sep 2014	1.58 (0.47, 5.29) p=0.463	2.32 (0.64, 8.40) p=0.20	1.58 (0.37, 6.71) p=0.54	0.98 (0.20, 4.72) p=0.98
Conceived Oct-Dec 2014	0.52 (0.15,1.82) p=0.31	0.48 (0.13, 1.73) p=0.26	0.25 (0.04, 1.46) p=0.12	0.18 (0.03, 1.09) p=0.062
Pseudo R^2	0.05	0.09	0.20	0.23

[a] Maternal variables include height, parity and education
[b] Infant variables include postnatal age, gestational age and sex
[c] All models control for village as a fixed effect
[d] OR (95% CI)

Table 3.8 Marginal odds of small-for-gestational age (SGA) for three-month conception periods estimated at the mean value of all covariates. P-values were derived from the post-estimation comparison of the log odds of SGA in each three-month conception period relative to the log odds of SGA for the overall sample

Three-Month Conception Period	Marginal Odds of SGA[a] *Model including food insecurity*	Marginal Odds of SGA[a] in *Model excluding food insecurity*
Conceived Nov–Dec 2013 (n=27)	1.01 (0.34, 2.68) p=0.99	1.51(0.50, 4.50) p=0.47
Conceived Jan-Mar 2014 (n=64)	1.31 (0.71, 2.44) p=0.39	1.39 (0.73, 2.64) p=0.32
Conceived Apr-Jun 2014 (n=40)	0.92 (0.42, 2.01) p=0.83	0.89 (0.38, 2.07) p=0.78
Conceived Jul-Sep 2014 (n=22)	1.59 (0.56, 4.52) p=0.38	1.47 (0.48, 4.50) p=0.50
Conceived Oct-Dec 2014 (n=20)	0.26 (0.06, 1.12) p=0.070	0.27 (0.06, 1.17) p=0.081
Overall sample Odds SGA/odds of not SGA	0.79 (0.60, 1.03)	0.79 (0.60, 1.03)

[a] OR (95% CI)

3.6 Discussion

In the present analyses, we examined whether there was monthly variation in early neonatal size by three-month periods of conception in a rural agrarian population in India. We observed that, after controlling for various time-invariant maternal, infant and socio-demographic factors, infants conceived between July and September 2014 (born between approximately April and June 2015) had early neonatal weights that were about 208 g lower than the overall sample mean weight, and infants conceived between April and June 2014 (born between approximately January and March 2015) had mean early neonatal lengths that were about 0.6 cm lower than the overall sample mean length. In secondary analyses of SGA as the dependent variable, the pattern of monthly differences was less clear. We observed that the greatest odds of SGA relative to the overall sample odds overlapped with the period of lowest early neonatal mean weights. This difference, however, was not statistically significant. Our findings lend new insights as to the potentially sizable monthly differences in early neonatal size by periods of conception in an agriculturalist community in rural India where irrigated agricultural practices are common. The underlying patterns of risk factors for poor health and nutritional status in this setting are likely to be less extreme than those in other well-studied settings, such as the Gambia, or even other parts of South Asia, where the agricultural systems are different (e.g. primarily rain-fed, different major crops, etc.). If and how patterns of risk factors for poor fetal growth varies throughout the year and, to what extent they are related to sensitive periods during gestation remains to be fully elucidated.

Early neonatal size is a reflection of growth during the fetal period, and thus a reflection of maternal health and nutritional status at conception, as well as nutrition and health insults that occurred during gestation. Although trajectories of fetal growth are not fully understood, ultrasound data support that the greatest fetal weight gains occur during the second half of pregnancy, especially during the third trimester [94, 140]. Placental development, which occurs during the first trimester of pregnancy, may also have an important influence on rates of fetal weight gain in the third trimester [141]. Thus, we interpreted factors that may affect weight in the first and third trimesters in infants conceived between July and September 2014.

Infants conceived between July and September 2014 experienced their first trimester between approximately July and November 2014 (monsoon and early winter months) and their third trimester between approximately January and May 2015 (late winter and early summer months. The monsoon period (July-September) is a documented period of risk for food insecurity and poor maternal health and nutritional status in various developing country settings [72]. Likewise, in Shivgarh, the monsoon period and early winter months encompass a period of potentially high risk for health and nutrition insults. During these months, women face heavy agricultural labor demands for rice paddy preparation and harvest activities. In rural areas of India, including Shivgarh, women do not typically alter their usual activities during pregnancy [39, 70]. The period preceding the rice harvest is also a time when agriculturalists in Shivgarh report risk for low food availability that occurs if supplies of wheat diminish while the rice crop is still in the field (**Chapter 2**). The late winter and early summer months are a time of year when rural agriculturalist face temperatures extremes, as well as high demands for agricultural labor for wheat crop maintenance (January-February), and harvest (March-April) (**Chapter 2**). Although not reported by agriculturalists in Shivgarh as a "hungry" season, patterns of household food supplies are not well understood in irrigated multi-crop systems. It is possible that, similar to the period immediately preceding the rice harvest, the months immediately preceding the wheat harvest may represent another period of diminished household food supplies, if the supply of rice diminishes prior to completion of the wheat harvest.

Periods of greatest fetal length gain are less well understood, but likely occur between mid, and possibly late pregnancy [94, 140]. Placental development during the first trimester may also influence rates of fetal linear growth in later pregnancy [142]. Therefore, we interpreted factors that may affect rates of length gain primarily during the first and second trimesters for infants conceived between April and June 2014. Infants conceived between April and June 2014 experienced their first trimester between approximately April and August 2014 (late summer and monsoon) and their second trimester between approximately July and November 2014 (monsoon and early winter). These infants would have been exposed to periods of potentially high environmental stress during both of these periods of their gestation. For example, these infants would have had some exposure to the monsoon period during both the first and second trimesters of pregnancy. They also would have had some exposure to the wheat harvest period, a period of high agricultural labor demands for women, during the first trimester.

Most available studies that have examined seasonal differences in birth size focus on the season of birth, rather than the season of conception. In one prospective study in rural central India (Pune, Maharashtra), however, Rao and colleagues examined both the season of birth and the percent exposure time to difference seasons during gestation. The lowest mean birthweights occurred in the winter season (October-January) and the highest mean birthweights occurred in the summer (February-May). The maximum difference between months was approximately 145 g [39]. The authors found that complete exposure to the winter season during gestation had a significant independent effect on birthweight of about 6 g (p=0.04). Infants born in summer months were exposed to the winter months for a large proportion of their second and early third trimesters, while infants born in winter months had some exposure to the winter season only in the later part of the third trimester.

In the MINIMat study in rural Bangladesh, compared to the hot and dry months (March-May), a non-significant trend in the direction of lower mean birthweights was reported for births that occurred during the monsoon (June-September) and winter (October-February) months [93]. In the rural Gambia, mean birthweights adjusted for infant sex were lowest at the start of the rainy season (June), the period corresponding to the beginning of the peak agricultural work season, relative to other months of the year [92]. The findings from these studies seem to suggest that exposure to the monsoon period during sensitive periods of gestation is a commonality across various studies conducted in developing countries.

In contrast to results from this previously published research, the lowest mean early neonatal weights in Shivgarh were observed during summer months (conceived between July and September 2014 and born between approximately April and June 2015). In addition, the magnitude of observed differences between months of maximum and minimum weights during the year appears larger than observed in other parts of South Asia. Previous research supports an association between monthly differences in birth size and nutrition determinants such as energy intake, physical activity and exposure to infections [37, 93, 143]. Comparisons across settings with different underlying contextual factors (e.g. crops grown, access to irrigation, female participation in agriculture, etc.), and thus different monthly or seasonal patterns of risk factors for poor health and nutritional status, may thus be inadequate.

Fewer studies have examined monthly differences in birth-length, but the magnitudes of reported length differences are within the range of those observed in Shivgarh. In rural central India, Rao et al (2009) reported birth-lengths that were approximately 1 cm lower in winter months (January) as compared to summer months, but did not examine this difference with reference to timing of exposure during gestation as they did for birthweight [39]. In MINIMat, Bangladesh, birth-lengths were on average approximately 0.5 cm lower among infants born in the November-January period as compared to other months [93]. Likewise in Shivgarh, infants born during winter months had the lowest mean early neonatal lengths (conceived between April and June 2014 and born between approximately January and March 2015). Also consistent with our findings are the observations from previously published research that the timing of the period with lowest mean birthweights does not coincide with the period of lowest mean birth-lengths [39, 93]. This provides support to previous findings that suggest that fetal weight and length growth are sensitive to environmental insults during different periods of gestation [94].

In this study, we observed consistency in the predictors of early neonatal weight and length and SGA. Among the time-invariant factors we examined, the statistically significant associations with measures of early neonatal size were in the direction expected, with the exception of maternal education. It is possible that important difference in attained levels of education existed in our sample, but we were unable to adequately control for these differences due to the imprecise measure of our education variable. We also observed a relatively strong association between primiparity and measures of early neonatal size (more than 300 g for weight and more than 1.0 cm for length) [144]. The reason for this large association is not known, but could be related to greater adaptations required by the mother for the first pregnancy exacerbated by poverty.

Food insecurity measured during the late third trimester of pregnancy and gestational age of the infant emerged as an important predictors of early neonatal size in all regression analyses. We considered the possibility that food insecurity and gestational age mediated the association between three-month conception periods and early neonatal size, but found no strong evidence for this in our models. We also tested for a statistical interaction between three-month periods of conception and food insecurity and three-month periods of conception and gestational age, but found no significant association between either of these interactions and early neonatal size. Some published literature from the Gambia shows variation in pre-term births (and gestational ages) that occurred throughout the year [95]. Our sample, however, consisted only of full-term infants. The variation in our gestational age variable may have been too small to observe differential effects by three-month periods of conception, had one existed. Furthermore, our sample size and/or proportion of food-insecure women were possibly too limited to see this association, if it existed.

Our food insecurity data were also limited to a single measure taken during late pregnancy, which may not be representative of food insecurity at conception or throughout gestation. The observed association between food insecurity and early neonatal size is, however, consistent with the generally accepted belief that access and availability to food, particularly at sensitive periods during gestation, is a key driver of fetal growth. In our sample, relative to being food secure, being food insecure (measured in late pregnancy) was associated with a decrease in mean early neonatal weights and lengths of nearly 200 g and 0.8 cm, respectively. According to our conceptual framework (**Figure 1.3**), food insecurity before or during gestation may affect fetal growth via an influence on maternal nutritional status. This possible mechanism, however, has not been well explored in the literature, and few studies in developing countries have examined the association of food insecurity during pregnancy with size at birth. Research among low-income women in developed countries does, however, support the relationship we observed [145].

This study has the advantage that it was nested within a prospective design in which pregnant women were recruited continuously over the course of 14 months. It was also conducted in a novel setting where irrigated agricultural practices are common. This study also has several limitations. We were able to collect valid anthropometric measures only for approximately 64% of the sample of all pregnant women identified in these nine selected villages. Our sample is thus not a universal sample and possibly not a representative sample of pregnant women from these villages. During some three-month conception periods, particularly between July and September 2014, the three-month conception period when we observed early neonatal weights that were significantly lower than the overall sample mean, our sample of births was very small. Comparisons of key characteristics between included and excluded participants overall and, by three-month conception periods, however, suggested negligible differences between the two groups. Therefore, the risk for selection bias in either the overall sample of measured infants, or differential selection bias by three-month periods of conception appears minimal (**Appendix B**). In our comparisons of key characteristics, however, we often did not have complete data available for participants that were not included in the present study. It is therefore possible that some differences existed between groups that we were not able to detect as a result of missing data. It is also possible that underlying seasonal patterns in conception and/or births may have resulted in a smaller number of infants conceived during the monsoon months. The numbers of births for primiparous mothers in India peaks during the monsoon months, approximately nine months following the peak marriage months (November-December) [125]. Possible seasonality of births for multiparous women (approximately 2/3 or our sample) is however, much less well understood. The consequence of such an underlying seasonal patterns, had it existed, could be that the group of infants conceived between July and August 2014 were a highly select group [146]. Thus, we cannot fully exclude the possibility that the results of these analyses are an artifact of selection bias.

Temporary refusal and unavailability of mothers was common, and due to logistical field constraints, teams of enumerators were often not able to re-visit the mother within seven days of birth. In our sample, 71% of infants measured at the scheduled birth visit were measured within seven days after birth (**Appendix B**). In developed countries, newborn infants generally lose weight in the first 72 hours after birth, and then regain their birthweight by about seven days [147]. Literature on postnatal weight loss in developing countries is, however, more limited, and prone to systematic sources of error (e.g. infants not weighed daily) [147, 148]. Some, but not all, of the available literature supports the existence of postnatal weight loss between birth and seven days, with a nadir on the third day. We did not observe a pattern of variation in early neonatal weight by age at measurement in our cross-sectional sample of infants measured between birth and seven days, for reasons that are unclear. In our sample, physiological weight loss and re-gain may occur later than three days after birth, as suggested in a few studies [147, 148]. Sensitivity analyses in which non-linear age terms (a quadratic age term and a categorical age term) were tested in separate analyses did not reveal any large differences in model parameters or model inference. Therefore, only a non-significant linear infant age term was included in final models (**Appendix B**). Lastly, to test our assumptions for the collapsing of consecutive conception months, we considered alternate monthly periods (e.g. by grouping consecutive months into two month, rather than three month clusters) and observed a negligible effect of these alternative variable specifications in analyses. To maximize sample size, we concluded that our choice of groupings for conception periods was appropriate.

In our sample, we had missing data in independent variables that were likely the result of logistical challenges in this field setting (e.g. field teams not able to carry heavy anthropometric equipment). Although we had complete birth data for infants in our sample, we had month of conception data for approximately 40 fewer participants due to missing values, or suspected errors in LMP data. These missing data were handled within Stata's full information maximum likelihood procedure, as previously described. Comparisons of key characteristics between participants with and without missing data, however, revealed negligible differences between the two samples, supporting our assumption of data MAR. Sensitivity analyses in which the full-information-maximum-likelihood procedure was not used to handle the missing data for infants measured within seven days of birth revealed similar results for all independent variables with slightly less statistical significance observed for the periods of conception variables. The lower level of statistical significance observed in these models may have been due to the reduced sample size that resulted from analyzing only complete cases. Assuming MAR, however, the likelihood of bias is greater for analyses that exclude subjects with incomplete data on independent variables. The full-information-maximum-likelihood approach within the SEM procedure in Stata cannot be applied to logistic regression, and thus, we were unable to conduct a sensitivity analysis for models of SGA as the dependent variable.

In conclusion, despite some study limitations, we have shown substantial monthly differences in early neonatal size that depended on the period of conception. These differences remain after controlling for various time-invariant factors that are known predictors of size at birth. Small size at birth has important implications for the future growth and development of the infant, and India has the largest number of SGA infants in the world. Future research should seek to better understand the mechanisms for monthly or seasonal variation in size at birth to inform potential programs and policies to ameliorate these differences in rural agrarian populations.

Chapter 4

Aim 2: Monthly variation in rates of weight and length growth in infants under six months of age in rural Uttar Pradesh

Madan EM, Haas JD, Frongillo EA, Kumar V, Kumar A, Menon P

4.1 Abstract

Physical growth is a useful and widely accepted marker of child health and nutritional status, especially in developing countries. The first *500* days (period from conception to approximately six months of age) is a critical period for growth and development, but relatively little is known about patterns of growth from birth to six months of infant age in low resource populations. In rural areas of developing countries, time of year when growth occurs may be associated with rates of infant growth. Pregnant women from nine purposefully selected villages in Uttar Pradesh were recruited continuously over 15 months to participate in a longitudinal study of infant growth. Descriptive analyses of attained size and growth velocity in three-month increments were conducted by infant age, sex, and month of the year starting the growth interval. Infants in our sample were, on average, growing below -1 SD from the Multicentre Growth Reference Study standard at all ages. Rates of length growth (cm/mo) were significantly lower than the overall sample mean rate of length growth when the 1-4 month interval of growth began in August 2015 (2.69 ± 0.031 cm/mo, p=0.013), September 2015 (2.71 ± 0.019 cm/mo, p=0.002;) or October 2015 (2.71± 0.027, p=0.03). Regardless of the month of year when growth began in any of the three-month growth intervals, no significant differences between rate of weight gain (g/mo) and the overall sample mean weight rate of weight gain was observed. Infants from

this understudied rural population in India were born small, and then grew poorly between birth and six months of age. In this context, the 1-4 month interval of growth may be a more sensitive period for detecting variation by time of year in rates of length growth. Context specific determinants of variation in infant growth throughout the year should be explored in future research.

4.2 Introduction

Physical growth is one of the most useful and widely accepted markers of child health and nutritional status. In India, child undernutrition, indicated by growth faltering is widespread. According to the National Family Health Survey-4 (NFHS-4), the prevalence of stunting, wasting and underweight in children less than five years of age in the state of Uttar Pradesh is 46.3%, 17.9% and 39.5%, respectively [116]. Although the prevalence of stunting has declined since 2005-06, the prevalence of wasting has actually increased [116].

Infants between birth and six months of age in developing countries are a particularly vulnerable group. They may be poorly endowed with nutrient reserves at birth, have high nutrition requirements for growth and development, and are completely dependent on the mother to meet their nutritional needs [16, 76]. Several previously conducted analyses that compare the growth of infants between birth and six months of age from developing countries to the 2006 WHO Multicentre Growth Reference Study (MGRS) standard have shown that growth faltering is already present at birth, and that the prevalence of undernutrition in this age group is much higher than previously thought [9, 12, 13].

A recent analysis of the cross-sectional National Family Health Survey-3

(NFHS-3) data from India shows that the prevalence of undernutrition, especially wasting, is actually higher in infants less than six months of age as compared to infants 6-59 months of age [12]. The *first 500 days* (conception through approximately six months of infant age) is increasingly recognized as a sensitive period to address growth and developmental deficits, yet infants less than six months of age have frequently been excluded from nutrition surveys and marginalized in nutrition programs [12, 16].

In much of rural India, regularly occurring nutritional stress associated with patterns in the climate and agricultural cycles may be important indirect determinants of early growth faltering, and/or failure to achieve nutritional recovery in early life [72, 73]. In tropical and sub-tropical regions of developing countries, monthly and seasonal variation in the growth of older children has been fairly well documented. Most of the of the available evidence suggests a decline in rates of growth that occur during "hungry" periods of the year, which often coincide with the rainy months leading up to the harvest [73, 98, 149-151]. This phenomenon in developing countries is thus typically attributed to monthly or seasonal variation in factors such as food availability and infectious disease [72, 73]. Differences throughout the year in the rates of infant growth between birth and six months of age, however, are poorly understood. Some previously published studies suggest that rates of growth differ throughout the year in this age group, while others show no association between month and season of the year with growth velocity [96-98, 152]. The large burden of undernutrition in early life in India and the susceptibility of poor agrarian populations to monthly or seasonal agro-climatic stress highlight the need to better understand the patterns of early infant growth throughout the year. The primary objective of this chapter was to describe patterns of weight and length growth (attained size and growth velocity) by age, sex and month of year for infants between birth and six months of age. The secondary objective was to explore whether growth during one or more three-month age intervals during the first six months of life (0-3, 1-4, 2-5, and 3-6 months) were more sensitive to the time of year when the growth interval began.

4.3 Methods

4.3.1 Subjects and sample

This longitudinal study was conducted in nine purposefully selected villages of the Shivgarh block of the Rae Bareli district in Uttar Pradesh, India. A description of the villages and summary of the study objectives and methods has been reported previously (**Chapter 2-3**). In brief, Shivgarh has a subtropical climate and is characterized by three main seasons: summer (April-June), monsoon (July-September) and winter (October-March) that vary in temperature and rainfall. The primary livelihoods are semi-subsistence farming and agricultural labor. The staple crops are rice and wheat, and peppermint is grown as a cash crop. Most farmers have access to irrigation via canals and tube wells. The two harvest periods for staple crops occur in October-November and March-April for rice and wheat, respectively, and represent periods of heavy labor demands for women.

From July 2014 to September 2015, all healthy pregnant women (n=599) in the 32nd week of pregnancy or later, residing in the nine villages were invited to participate in this study. Pregnant women were enrolled and scheduled to be visited a total of eight times: during late pregnancy (enrollment), at birth, monthly from 1-6 months of infant age and then again at nine and 12 months of infant age, as described in Chapter 2 and 3.

At each visit, a team of enumerators administered structured questionnaires to the mother and the head of the household or other knowledgeable household member. Child anthropometry was collected monthly between birth and six months of infant age using standard equipment and techniques that were described in Chapter 2-3. At each visit, infant weight and length values were measured independently by two enumerators and were averaged for use in analyses. Infant weights were corrected for any clothing worn during measurement as previously described (**Chapter 2**).

Data were scrutinized within and between visits for biologically implausible measures in weight and length (likely due to measurement and recording errors). To identify extreme values, raw attained weight and length values were converted to age and sex specific Z-scores based on the MGRS standard [9]. Outlier Z-score values were defined according to the following criteria: length-for-age Z-scores (LAZ) less than -6 or greater than 6; weight-for-age Z-scores (WAZ) less than -6 or greater than 5; weight-for-length Z-scores (WLZ) less than -5 or greater than 5 [124]. Outlier Z-scores or otherwise implausible data values were excluded from the analyses (n=23 length values and n=13 weight values).

Infants were classified as stunted, wasted or underweight if their LAZ, WLZ or WAZ, respectively, were < -2-Z-scores from the MGRS standard median. Preterm infants (less than 37 weeks) are expected to have different patterns of postnatal growth as compared to term infants (greater than or equal to 37 weeks), and thus, the present analyses pertain only to the growth data for term singleton infants collected between birth and six months of infant age [118]. The International Food Policy Research Institute (IFPRI) and the Community Empowerment Lab (CEL) ethical review boards provided ethical approval for this study, following guidelines for the Helsinki Declaration of 1975 as revised in 1983 [134].

4.4 Statistical analyses

To account for different levels of variability in growth by age, Stata's *mixed* procedure (version 13) was used to generate individual- level empirical Bayes estimates of slopes of size by age in each of the four-growth intervals (0-4 mo, 1-4 mo, 2-5 mo, 3-6 mo) (**Appendix C**) [153]. In these models, infant weight and length within an interval were considered separately as the dependent variables, infant age was considered as a fixed effect, and both infant age and identification number (uniquely identified each infant) were considered as random effects. Only data for the 361 infants who had at least two valid measures for weight or length in any of the four growth intervals were included in the present analyses. We considered three conditions when establishing this criterion. First, growth over the entire first six months of life is not linear. Due to the fact that we were estimating slopes over smaller, and thus more linear age increments for growth, a minimum of two measurements was required to generate a slope. Second, individual-level slopes estimated for infants with either three or four measures in an interval were not significantly different[7] from slopes estimated using only two data points. Lastly, whether growth measures were consecutive (e.g. only a birth and a one month measure, only a two- and a three- month measure etc.), or distributed across the

[7] $p>0.05$ in a two-sample t-test

interval (e.g. a birth and a two-month measure or a one- and a three-month measure), made no significant difference[8] in the estimates of slope. The infants included in the analyses had an average of five (range 2-7) valid measures recorded between birth and six months of age. Descriptive analyses were conducted for both attained infant size and infant growth velocity by age, sex and month of year. The individual infant weight and length slopes generated from the *mixed* procedure in Stata were then considered separately as dependent variables in multivariable regression analyses for each growth interval. Sex of the child and the month at the beginning of the growth interval were considered as independent variables.

Following regression models, for each three-month infant growth interval, Stata's post-estimation procedure, *lincom*, was used to estimate marginal means of weight and length velocity for each month of the year starting a growth interval [153]. The post-estimation procedure analyzed the stored results of the regression models. The *lincom* procedure was then used to test for differences between marginal means and the overall sample means for models of weight and length velocity, separately.. Marginal means were estimated because we were interested in the mean values of weight and length velocity adjusted for other model covariates. We compared estimated marginal means of weight and length velocity at each month of the year starting a growth interval to the overall sample mean because this difference was thought to be a more meaningful reflection of differences throughout the year as compared to between month comparisons. All analyses were conducted using Stata version 13 (StataCorps, TX). Statistical significance was defined as $p<0.05$.

[8] $p > 0.05$ in a two-sample t-test

4.5 Results

The 461 infants who were measured at least once during the first six postnatal months of life were included in analyses of attained size. A sub-sample of 361 infants who had at least two measurements taken in any one of the four three-month intervals of growth were included in longitudinal analyses of at least one-growth interval (78.3% of attained growth sample) (**Table 4.1**).

Attained weight and length of infants increased with age for both sexes and clustered below the median of the MGRS standard. With the exception of birth-length, average attained weight and length at each age was less than or equal to -1 SD of the MGRS standard median (**Table 4.2; Figure 4.1; Figure 4.2**). Female infants, on average, were lighter and shorter than male infants at all ages. Relative to the MGRS standard, mean length-for-age Z-scores (LAZ) were between -1.25 and -1.48, mean weight-for-age Z-scores (WAZ) were between -1.73 and 1.80, and mean weight-for-length Z-scores (WLZ) were between -0.91 and -1.07. At birth (within the first seven days of life), the prevalences of stunting, wasting and underweight were 23.9%, 25.0% and 30.0%, respectively (**Table 4.3**). Compared to the prevalences of undernutrition at birth, at one month of age the prevalences of both stunting and underweight were slightly higher (28.3% and 39.8%, respectively), and the prevalence of wasting was substantially lower (17.1%). Prevalences of all three nutrition indicators remained fairly constant between one and six months of infant age (**Figure 4.3**). At all infant ages, except at three and six months of age, mean weight-for-length Z-scores tended to be below the age specific overall sample mean in either July 2015 or August 2015 ($p<0.1$) (**Table 4.4**).

Both male and female infants had mean weight and length velocities that were, on average, below the MGRS median. Weight and length velocity decreased as the age of the infants starting the interval increased. Relative to male infants, female infants had, on average, lower weight and length velocities during all four-growth intervals (**Table 4.5**). For weight velocity, there was no consistent pattern for month/s of the year when rate of growth was either highest or lowest for any of the three-month growth intervals (**Table 4.6).** For length velocity in all four-three-month growth intervals, the lowest rate of growth occurred when the interval started in either August or September 2015. There was no clear pattern for months of the year when rate of length growth was highest.

Table 4.1 Number of infants measured at each age, and the number of these infants with sufficient growth measures to be included in analyses of weight and length velocity for each three-month growth interval

Infant age (mo)[a]	Number of valid anthropometry measurements at each infant age	Number of valid weight and length velocity estimates during each growth interval[b]			
		Age interval (mo)			
		0-3	1-4	2-5	3-6
0	225	213	206	195	171
1	350	274	266	247	223
2	333	283	279	270	228
3	328	277	278	275	244
4	257	208	216	217	214
5	247	198	202	209	208
6	283	229	234	237	244
Total infants with attained size/slope estimate	461	342	332	321	286
Total Infants with < 2 growth measures		88	108	130	164

[a] 0: 0 d ≤ age ≤ 7 d; 1: (0.5 mo ≤ age ≤ 1.5 mo); 2: 1.5 mo ≤ age < 2.5 mo; 3: (2.5 mo ≤ age < 3.5 mo); 4: (3.5 mo ≤ age < 4.5 mo); 5: (4.5 mo ≤ age < 5.5 mo); 6: (5.5 mo ≤ age < 6.5 mo)
[b] Estimates for rates of growth were valid if an infant had at least two measures of either weight or length in any of the four age intervals

Table 4.2 Attained size for infants between birth and six months of age, by age and sex, in a sample of infants from Shivgarh, Uttar Pradesh and in the Multicentre Growth Reference Study (MGRS) standard

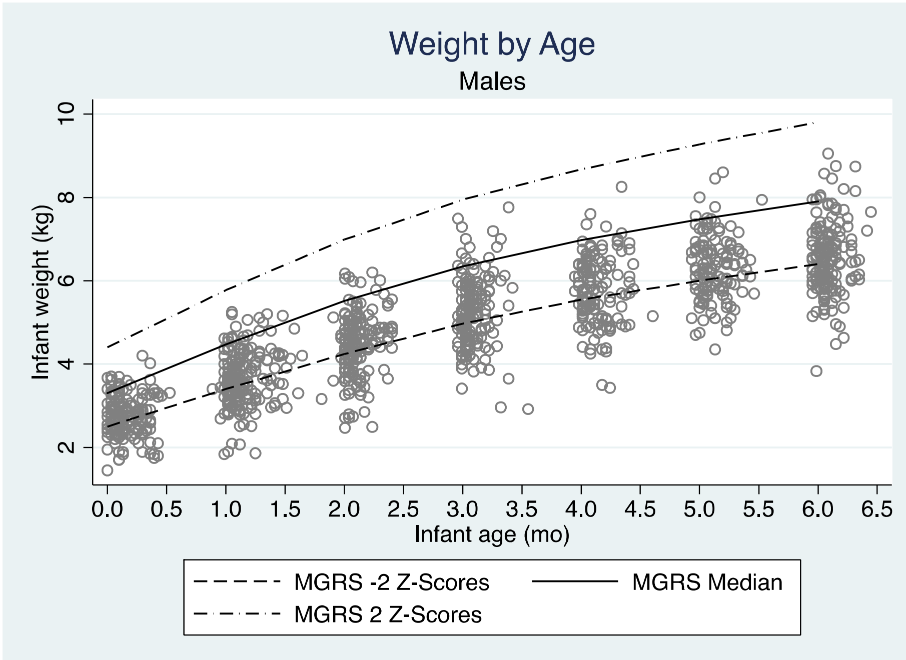
	Attained Weight, kg				Attained Length, cm			
	Boys		Girls		Boys		Girls	
Infant age (mo)	Sample[a]	MGRS[b]	Sample[a]	MGRS[b]	Sample[a]	MGRS[b]	Sample[a]	MGRS[b]
0	2.8 ± 0.5 (n=109)	3.3-0.4	2.6 ± 0.5 (n=111)	3.2 -0.4	48.2 ± 2.2 (n=111)	49.9-1.9	47.7 ± 2.2 (n=111)	49.1-1.8
1	3.7 ± 0.7 (n=188)	4.5-0.4	3.4 ± 0.6 (n=159)	4.2 -0.6	52.5 ± 2.7 (n=189)	54.7-1.9	51.5 ± 2.5 (n=157)	53.7-2.0
2	4.5 ± 0.7 (n=173)	5.6 -0.7	4.2 ±0.6 (n=154)	5.1 -0.6	56.1 ± 2.8 (n=179)	58.4-2.0	55.0 ± 2.4 (n=152)	57.1-2.1
3	5.3 ± 0.8 (n=170)	6.4-0.7	4.8 ± 0.7 (n=156)	5.8 -0.6	58.9 ± 2.4 (n=170)	61.4-2.0	57.5 ± 2.2 (n=154)	59.8-2.1
4	5.8 ± 0.8 (n=138)	7.0 -0.8	5.3 ± 0.7 (n=118)	6.4 -0.7	61.0 ± 2.5 (n=139)	63.9-2.1	59.5 ± 2.3 (n=113)	62.1-2.2
5	6.3 ± 0.8 (n=135)	7.5-0.8	5.6 ± 0.8 (n=109)	6.9 -0.8	63.1 ± 2.4 (n=134)	65.9-2.1	61.4 ± 2.3 (n=110)	64.0-2.2
6	6.6 ± 0.9 (n=161)	7.9-0.8	6.0 ± 0.8 (n=121)	7.3 -0.8	64.3 ± 2.3 (n=156)	67.6 -2.1	62.9 ± 2.1 (n=121)	65.7-2.2

[a] Mean ± SD
[b] MGRS median -1SD; Only the minus 1 standard deviation is reported because the MGRS reference population does not have a symmetrical distribution

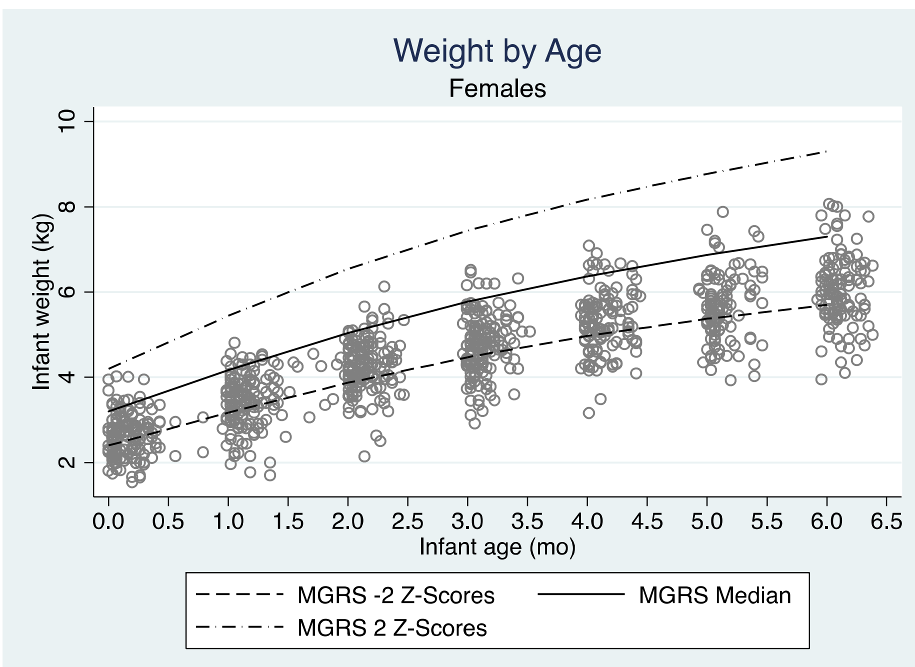
Table 4.3 Weight-for-Age Z-scores, length-for-age Z-scores and weight-for-length Z-scores and prevalences of underweight, stunting and wasting by age in a sample of infants from Shivgarh, Uttar Pradesh

	Height-for-age Z-scores	Weight-for-age Z-scores	Weight-for-length Z-scores	Undernutrition (%)			
Infant age, mo	Sample[a]	Sample[a]	Sample[a]	Stunted[b]	Underweight[c]	Wasted[d]	Severely wasted[e]
0	-1.11 ± 1.15 (n= 222)	-1.42 ± 1.17 (n=220)	-1.19 ± 1.50 (n=200)	23.9 (n=53)	30.0 (n=66)	25.0 (n=50)	13.5 (n=27)
1	-1.40 ± 1.29 (n= 347)	-1.79 ± 1.26 (n= 348)	-0.91 ± 1.26 (n=340)	28.5 (n=99)	39.9 (n=139)	17.1 (n=58)	5.3 (n=18)
2	-1.25 ± 1.26 (n= 330)	-1.80 ± 1.13 (n=326)	-0.97 ± 1.13 (n=324)	23.8 (n=79)	38.1 (n=125)	18.1 (n=59)	4.3 (n=14)
3	-1.31 ± 1.09 (n= 325)	-1.76 ± 1.17 (n=326)	-0.95 ± 1.15 (n=323)	25.2 (n=82)	39.6 (n=129)	16.7 (n=54)	5.3 (n=17)
4	-1.42 ± 1.14 (n= 255)	-1.75 ± 1.15 (n=256)	-0.97 ± 1.07 (n=254)	31.0 (n=79)	39.1 (n=100)	16.9 (n=43)	3.5 (n=9)
5	-1.35 ± 1.06 (n=246)	-1.75 ± 1.09 (n= 244)	-1.07 ± 1.05 (n=243)	25.6 (n=63)	41.0 (n=100)	17.7 (n=43)	4.5 (n=11)
6	-1.48 ± 1.04 (n=282)	-1.73 ± 1.14 (n= 282)	-0.99 ± 1.12 (n=281)	30.5 (n=86)	38.7 (n=109)	17.1 (n=48)	5.0 (n=14)

[a] Mean ± SD
[b] < -2 SD of MGRS length-for-age Z-score median
[c] < -2 SD of MGRS weight-for-age Z-score median
[d] < -2 SD of MGRS weight-for-length Z-score median
[e] < -3 SD of MGRS weight-for-length Z-score median

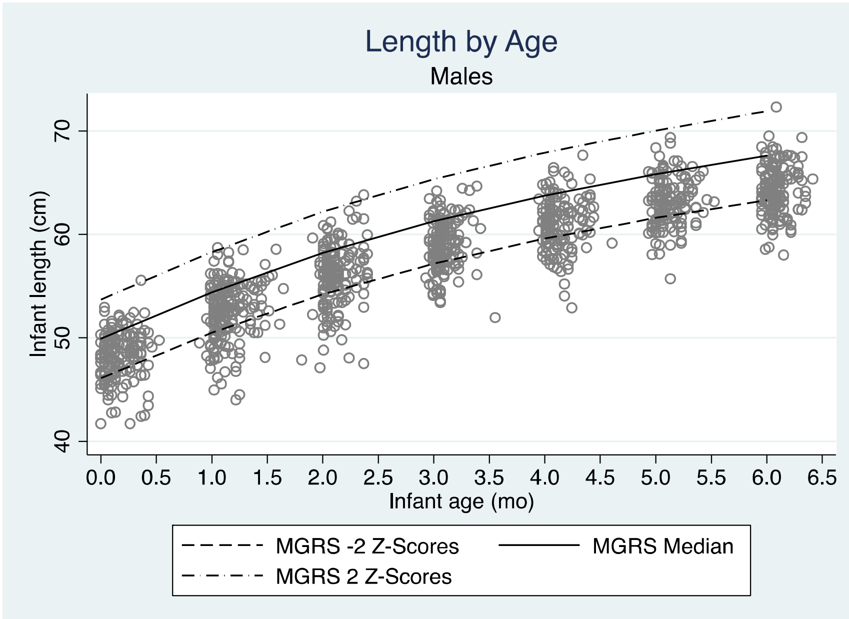


(A)

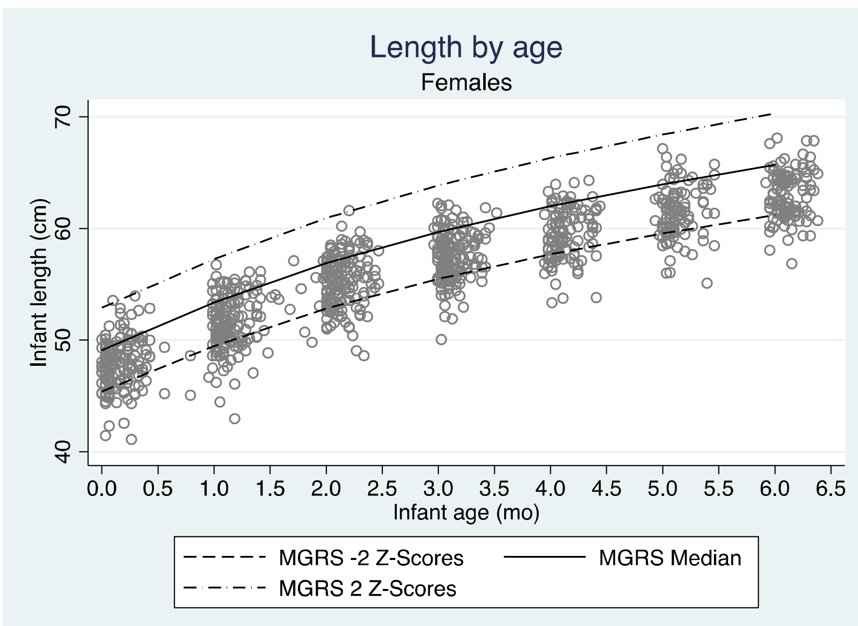


(B)

Figure 4.1 Weight by age for male (A) and female (B) infants relative to the Multicentre Growth Reference Study (MGRS) standard



(A)



(B)

Figure 4.2 Length by age for male (A) and female (B) infants relative to the Multicentre Growth Reference Study (MGRS) standard

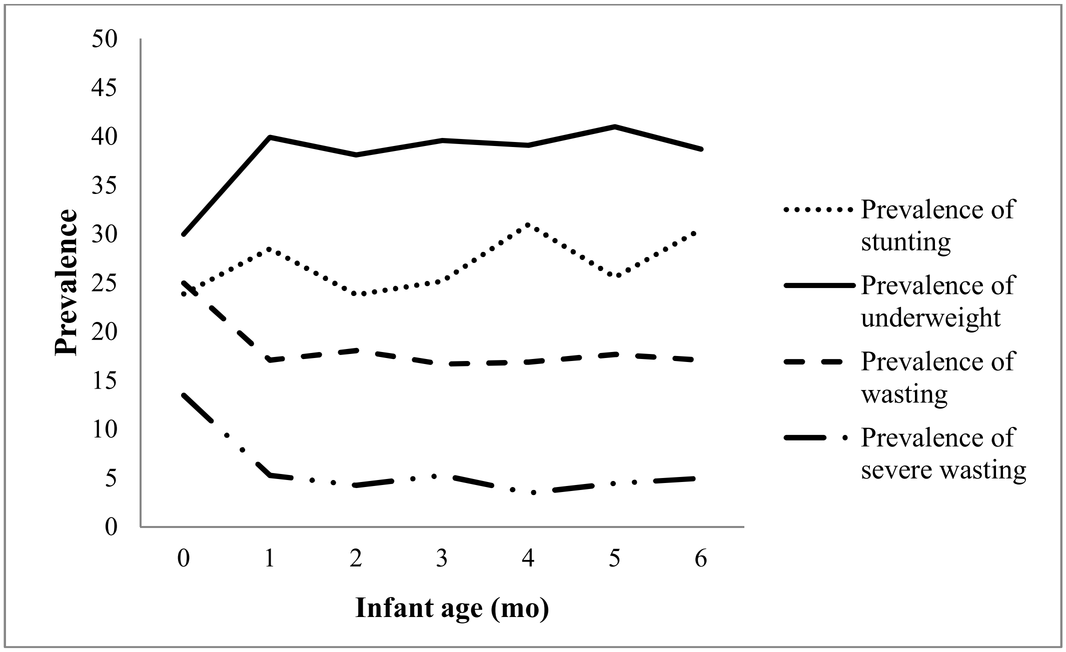


Figure 4.3 Prevalence of stunting, underweight, wasting and severe wasting by age between birth and six month in Shivgarh, Uttar Pradesh

Table 4.4 Marginal means of weight-for-length Z-scores by month of year for infants 0-6 months of age in Shivgarh. P-values are derived from the post-estimation comparison of marginal means to the overall sample mean for each age[a]

	Weight-for-Length Z-score						
	Infant Age (mo)						
Month of year	0[a]	1[a]	2[a]	3 [a] (n=323)	4[a] (n=254)	5 [a] (n=243)	6 [a] (n=281)
Aug 2014	-1.84 ± 0.53 p=0.22	---	---	---	---	---	---
Sept 2014	-1.78 ± 0.31 ***p=0.055***[b]	-1.02 ± 0.37 p=0.76	---	---	---	---	---
Oct 2014	-1.15 ± 0.28 p=0.91	-1.37 ± 0.27 ***p=0.095***	-1.19 ± 0.37 p=0.55	---	---	---	---
Nov 2014	-1.02 ± 0.30 p=0.58	-0.65± 0.25 p=0.29	-0.83 ± 0.24 p=0.56	-0.64 ± 0.66 p=0.64	---	---	---
Dec 2014	-0.58 ± 0.378 p=0.112	-0.73± 0.23 p=0.44	-.094 ± 0.21 p=0.89	-0.81 ± 0.24 p=0.56	-0.92 ± 0.33 p=0.90	---	---
Jan 2015	-0.49 ± 0.39 p=0.075	-0.81 ± 0.27 p=0.72	-1.16 ± 0.21 p=0.36	-1.11 ± 0.22 p=0.46	-1.00 ± 0.28 p=0.90	-1.00 ± 0.37 p=0.83	---
Feb 2015	-1.29 ± 0.32 p=0.74	-0.91± 0.231 p=0.99	-.0814 ± 0.22 p=0.49	-0.97 ± 0.21 p=0.91	N/A[c]	N/A	-1.09 ± 0.36 p=0.76
Mar 2015	-0.04 ± 0.41 p=0.05	-0.55 ± 0.22 p=0.104	-0.561± 0.24 p=0.094	-0.52 ± 0.24 p=0.069	N/A	N/A	-0.08 ± 0.34 p=0.49

Table 4.4 (continued)

Apr 2015	-1.68 ± 0.50 p=0.32	-1.47 ± 0.27 ***p=0.042***	-0.80 ± 0 .21 p=0.43	-0.90 ± 0.24 p=0.79	-1.23± 0.23 p=0.24	-1.04 ± 0.25 p=0.88	-1.09 ± 0.36 p=0.76
May 2015	-1.75 ± 0.63 p=0.37	-0.614 ± 0.34 p=0.38	-1.10 ± 0.24 p=0.56	-0.98 ± 0.23 p=0.92	-.891 ± 0.23 p=0.74	-1.01 ± 0.21 p=0.75	-1.08 ± 0.22 p=0.68
Jun 2015	-1.52 ± 0.41 p=0.410	-0.83 ± 0.35 p=0.82	-0.94± 0.28 p=0.92	-1.40 ± 0.29 p=.117	-1.11± 0.20 p=0.46	-0.95 ± 0.21 p=0.56	-1.23± 0.22 p=0.27
Jul 2015	-2.68 ± 0.70 ***p=0.036***	-1.49 ± 0.34 ***p=0.089***	*-0.713 ± 0 .416* p=0.55	-0.974 ± 0.36 p=0.95	-1.40 ± 0.25 ***p=0.085***	-0.85± 0.27 p=0.40	-1.00 ± 0.25 p=0.97
Aug 2015	-0.09 ± 0.36 p=0.58	-0.98 ± 0.50 p=0.892	-1.75 ± 0.31 ***p=0.011***	-1.21 ± 0.38 p=0.505	-1.02± 0.30 p=0.863	-1.72± 0.27 ***p=0.018***	-0.84 ± 0.22 p=0.495
Sep 2015	-0.37 ± 0.45 p=0.068	-0.97 ± 0.25 p=0.825	-1.35 ± 0.33 p=0.245	-1.07 ± 0.26 p=0.638	-0.05 ± 0.29 p=0.081	-1.36 ± 0.31 p=0.36	-1.36 ± 0.23 p=.103
Oct 2015	-1.39± 0.704 p=0.77	-0.65± 0.37 p=0.70	-1.02 ± 0.23 p=0.80	-0.72 ± 0.33 p=0.48	-1.12 ± 0.23 p=0.49	-.754 ± 0.33 p=0.326	-0.90 ± 0.29 p=0.73

Table 4.4 (continued)

Nov 2015	---	---	-0.53 ± 0.29 p=0.138	-0.94 ± 0.21 p=0.94	-0.62 ± 0.33 p=0.29	-1.35 ± 0.23 p=0.23	-0.66 ± 0.31 p=0.30
Dec 2015	---	---	-0.19 ± 0.32 p=0.015	-0.86 ± 0.30 p=0.77	-0.65 ± 0.20 p=0.116	-0.84 ± 0.30 p=0.42	-0.90 ± 0.22 p=0.67
Jan 2016	---	---	---	-0.40 ± 0.36 p=0.132	-0.52 ± 0.27 p=0.095	-.008 ± 0.20 p=0.18	-0.71 ± 0.31 p=0.38
Feb 2016	---	---	---	---	-0.04 ± 0.28 p=0.058	-0.79 ± 0.27 p=0.277	-0.77 ± 0.21 p=0.297
Mar 2016	---	---	---	---	---	-0.87 ± 0.31 p=0.52	-0.67 ± 0.31 p=0.313
Apr 2016	---	---	---	---	---	---	-0.83 ± 0.31 p=0.62
Overall sample	-1.19 ± 0 .11	-0.91 ± 0.07	-0.97± 0.06	-0.95 ± 0.06	-0.97 ±0.07	-1.08 ± 0.07	-0.99 ± 0.07

[a] Mean ± SE
[b] P-values in bold italics are those for growth velocities that are significantly lower (p<0.05) than the overall sample mean
[c] N/A means that zero infants in this month had valid weight-for-length Z-score values

Table 4.5 Mean weight and length velocity by three-month age intervals of growth for infants 0-6 months of age, by sex, in Shivgarh, Uttar Pradesh

	Weight velocity (g/mo)				Length velocity (cm/mo)			
	Boys		Girls		Boys		Girls	
Age interval (mo)	Sample [a]	MGRS [b]	Sample [a]	MGRS [b]	Sample [a]	MGRS [b]	Sample [a]	MGRS [b]
0-3	836 ± 133 (n=177)	996 -187	766 ± 111 (n=162)	868 -172	3.5 ± 0.1 (n=179)	3.8 -0.4	3.4 ± 0.1 (n=162)	3.5 -0.4
1-4	712 ± 92 (n=175)	855 -172	657 ± 82 (n=157)	751 -151	2.8 ± 0.1 (n=174)	3.2 -0.4	2.8 ± 0.1 (n=156)	2.9 -0.4
2-5	566 ± 81 (n=168)	671 -152	510 ± 82 (n=148)	606 -132	2.3 ± 0.2 (n=170)	2.5 -0.4	2.2 ± 0.2 (n=147)	2.4 -0.4
3-6	456 ± 89 (n=156)	527 -134	410 ± 90 (n=130)	493 -120	1.9 ± 0.2 (n=154)	2.1 -0.4	1.8 ± 0.2 (n=129)	2.0 -0.4

[a] Mean ± SD

[b] MGRS median (-1SD); Only the minus 1 standard deviation is reported because the MGRS reference population does not have a symmetrical distribution

Table 4.6 Mean weight and length velocity by month at start of the growth interval of growth for infants 0-6 months of age in Shivgarh, Uttar Pradesh

	Weight velocity (g/mo)				Length velocity (cm/mo)			
	Growth interval (mo)				Growth interval (mo)			
Start of growth interval (mo)	0-3[a]	1-4 [a]	2-5 [a]	3-6 [a]	0-3 [a]	1-4 [a]	2-5 [a]	3-6 [a]
Aug 2014	814 ± 98 (n=15)	---	---	---	3.48 ± 0.142 (n=15)	---	---	---
Sep 2014	820 ± 158 (n=28)	691 ± 71 (n=13)	---	---	3.47 ± 0.135 (n=29)	2.74 ± 0.171 (n=13)	---	---
Oct 2014	775 ±146 (n=33)	697 ± 109 (n=26)	516 ± 66 (n=12)	---	3.45 ± 0.159 (n=33)	2.76 ± 0.069 (n=26)	2.20 ± 0.120 (n=12)	---
Nov 2014	770 ± 1301 (n=32)	689 ± 94 (n=29)	529 ± 84 (n=23)	405 ± 51 (n=8)	3.43 ± 0.165 (n=32)	2.79 ± 0.069 (n=28)	2.24 ± 0.182 (n=23)	1.87 ± 0.069 (n=7)
Dec 2014	797 ± 122 (n=28)	681 ± 86 (n=32)	536 ± 62 (n=24)	426 ± 83 (n=14)	3.50 ± 0.143 (n=27)	2.80 ±0.088 (n=32)	2.26 ± 0.104 (n=23)	1.87 ± 0.172 (n=14)
Jan 2015	793 ± 141 (n=28)	687 ± 92 (n=28)	548 ± 81 (n=29)	467 ± 117 (n=8)	3.48 ± 0.148 (n=28)	2.81 ± 0.122 (n=27)	2.28 ± 0.183 (n=29)	1.93 ± 0.209 (n=7)
Feb 2015	810 ± 144 (n=35)	674 ± 116 (n=25)	543 ± 116 (n=28)	421.3 ±101 (n=26)	3.51 ± 0.152 (n=35)	2.77 ± 0.112 (n=25)	2.34 ± 0.280 (n=27)	1.83 ± 0.206 (n=26)
Mar 2015	802 ± 116 (n=24)	669 ± 106 (n=35)	530 ± 96 (n=25)	407± 107 (n=27)	3.54 ± 0.133 (n=25)	2.79 ± 0.102 (n=35)	2.28 ± 0.272 (n=25)	1.91 ± 0.228 (n=27)
Apr 2015	829 ± 95 (n=16)	686 ± 79 (n=23)	536 ± 89 (n=31)	411 ± 81 (n=26)	3.50 ± 0.125 (n=17)	2.79 ± 0.111 (n=23)	2.27 ± 0.198 (n=32)	1.84 ± 0.202 (n=26)

Table 4.6 (continued)

May 2015	799 ± 92 (n=12)	668 ± 82 (n=15)	534 ± 86 (n=21)	450 ± 103 (n=30)	3.53 ± 0.141 (n=12)	2.73 ± 0 .099 (n=15)	2.34 ± 0.195 (n=22)	1.85 ± 0.184 (n=29)
Jun 2015	821 ± 94 (n=19)	717± 68 (n=12)	532 ± 67 (n=16)	416 ± 94 (n=22)	3.56 ± 0.133 (n=19)	2.84 ± 0.134 (n=12)	2.23 ± 0.176 (n=16)	1.84 ± 0.200 (n=22)
Jul 2015	832 ± 140 (n=11)	687± 90 (n=23)	543 ± 87 (n=12)	439 ± 89 (n=16)	3.44 ± 0.147 (n=11)	2.75 ± 0.107 (n=23)	2.18 ± 0.161 (n=12)	1.89 ± 0.192 (n=16)
Aug 2015	793 ± 123 (n=29)	694 ± 91 (n=12)	527 ± 90 (n=24)	432 ± 94 (n=13)	3.42 ± 0.132 (n=29)	2.69 ± 0.088 (n=12)	2.20 ± 0.181 (n=25)	1.76 ± 0.154 (n=13)
Sep 2015	822 ± 139 (n=16)	683 ± 87 (n=30)	560 ± 78 (n=13)	453 ± 96 (n=25)	3.49 ± 0.143 (n=16)	2.71 ± 0.113 (n=30)	2.16 ± 0.222 (n=13)	1.85 ± 0.121 (n=25)
Oct 2015	838 ± 112 (n=13)	705 ± 89 (n=16)	556 ± 77 (n=29)	448 ± 87 (n=13)	3.47 ± 0.137 (n=13)	2.71± 0 .107 (n=16)	2.21 ± 0.172 (n=29)	1.90 ± 0.235 (n=13)
Nov 2015	---	706 ± 77 (n=13)	547 ± 112 (n=16)	456 ± 75 (n=29)	---	2.76 ± 0.132 (n=13)	2.24 ± 0.153 (n=16)	1.85 ± 0.174 (n=29)
Dec 2015	---	---	561 ± 81 (n=13)	457 ± 92 (n=16)	---	---	2.33 ± 0.209 (n=13)	1.91 ± 0.130 (n=16)
Jan 2016	---	---	---	454 ± 74 (n=13)	---	---	---	1.96 ± 0.158 (n=13)

[a] Mean ± SE

In regression models for male and female infants combined, female sex was negatively associated with both weight and length velocity in all growth intervals ($p<0.05$), except for length velocity in the 1-4 month interval ($p=0.175$) (**Appendix C**). Mean rate of weight gain during any three-month interval did not differ from the overall sample mean rate of weight gain regardless of the month of year when the growth interval began (**Table 4.5**). In the 3-6-month growth interval, when growth began in March 2015, however, the difference in rate of weight growth relative to overall sample mean rate of weight growth approached statistical significance (-31g/mo; $p=0.067$).

In all three-month growth intervals, there was a tendency for significantly lower monthly rate of length gain relative to the overall sample rate of length growth when the growth interval began between August and October 2015. The statistical significance of these differences was most pronounced in the 1-4 month growth interval. Between one and four months of age, length velocity was significantly lower than the overall sample mean length velocity when growth began in August 2015 (2.69 ± 0.031 cm/mo, $p= 0.013$), September 2015 (2.71 ± 0.019 cm/mo, $p=0.002$) or October 2015 (2.71 ± 0.027 cm/mo, $p=0.03$). Infants who began any of the three-month growth intervals between approximately January 2015 and June 2015 tended to have length velocities that were equal to or greater than the overall sample mean length velocity.

Table 4.7 Marginal means of weight and length velocity by month at the start of the growth interval for infants 0-6 months of age in Shivgarh estimated at the mean value of infant sex. P-values were derived from the post-estimation comparison of marginal means to the overall sample mean in each age interval[a]

Start of growth interval (mo)	Weight velocity (marginal mean ± SE)				Length velocity (marginal mean ± SE)			
	Age interval (mo)				Age interval (mo)			
	0-3 [b] (n=339)	1-4 [b] (n=332)	2-5 [b] (n=316)	3-6 [b] (n=286)	0-3 [b] (n=341)	1-4 [b] (n=330)	2-5 [b] (n=317)	3-6 [b] (n=283)
Aug 2014	828 ± 32 p=0.44	---	---	---	3.49 ± 0.036 p= 0.78	---	---	
Sep 2014	826 ± 23 p=0.32	704 ± 25 p=0.47	---	---	3.48 ± 0.025 p=0.83	2.75 ± 0.030 p=0.49	---	---
Oct 2014	771 ± 22 p=0.14	701 ± 17 p=0.41	532 ± 24 p=0.75	---	3.45 ± 0.024 p=0.15	2.76 ± 0.021 p= 0.70	2.22 ± 0.057 p=0.46	---
Nov 2014	770 ± 22 p=0.13	686 ± 16 p=0.98	534 ± 17 p=0.74	413 ± 32 p=0.49	3.43 ± 0.024 ***p=0.031***	2.79 ± 0.020 p=0.32	2.24 ± 0.041 p=0.63	1.89 ± 0.069 p=0.69
Dec 2014	790 ± 23 p=0.60	681 ± 16 p 0.72	534 ± 17 p=0.71	425 ± 24 p=0.66	3.49 ± 0.026 p=0.782	2.80 ± 0.019 p=0.045	2.26 ± 0.040 p=0.97	1.87 ± 0.048 p=0.92
Jan 2015	789 ± 23 p=0.56	682 ± 17 p=0.81	549 ±15 p=0.55	470 ± 32 p=0.28	3.48 ± 0.026 p=0.89	2.81 ± 0.020 p=0.056	2.29 ± 0.036 p=0.46	1.93 ± 0.069 p=0.35
Feb 2015	806 ± 21 p=0.87	672 ± 18 p=0.42	538 ± 16 p=0.94	420 ± 18 p=0.34	3.51 ± 0.023 p=0.33	2.77 ± 0.021 p=0.84	2.34 ± 0.038 p=0.04	1.83 ± 0.036 p=0.29
Mar 2015	810 ± 25 p=0.78	669 ±15 p=0.24	528 ±17 p=0.48	404 ± 17 p=0.067	3.55 ± 0.027 p=0.010	2.79 ± 0.018 p=0.18	2.28 ± 0.039 p=0.62	1.90 ± 0.035 p=0.28
Apr 2015	830 ± 31 p=0.38	691 ±18 p=0.79	535 ±15 p=0.75	410 ± 18 p=0.15	3.50 ± 0.033 p=0.561	2.79 ± 0.022 p=0.29	2.27 ± 0.035 p=0.79	1.84 ± 0.036 p=0.43

Table 4.7 (continued)

May 2015	806 ± 36 p=0.92	671 ± 23 p=0.52	540 ± 18 p=0.99	45 ± 16 p=0.33	3.54 ± 0.040 p=0.18	2.74 ± 0.027 p=0.26	2.35 ± 0.041 p=0.04	1.85 ± 0.033 p=0.66
Jun 2015	817 ± 28 p=0.62	723 ± 26 p=0.148	534 ± 21 p=0.79	423 ± 19 p=0.51	3.56 ± 0.031 p=0.019	2.84 ± 0.031 p=0.013	2.24 ± 0.049 p=0.65	1.85 ± 0.039 p=0.67
Jul 2015	830 ± 37 p=0.47	680 ± 19 p=0.73	549 ± 24 p=0.69	442 ± 22 p=0.77	3.44 ± 0.041 p=0.27	2.74 ± 0.022 p=0.31	2.19 ± 0.057 p=0.219	1.90 ± 0.045 p=0.47
Aug 2015	791 ± 23 p=0.60	691 ± 26 p=0.84	520 ± 17 p=0.24	440 ± 25 p=0.85	3.42 ± 0.025 ***p=0.017***	2.69 ± 0.031 ***p 0.013***	2.20 ± 0.039 p=0.13	1.77 ± 0.050 ***p=0.07***
Sep 2015	818 ± 31 p=0.62	683 ± 16 p=0.84	556 ± 23 p=0.49	449 ± 18 p=0.44	3.48 ± 0.034 p=0.982	2.71 ± 0.019 ***p=0.002***	2.16 ± 0.054 ***p=0.07***	1.85 ± 0.036 p=0.67
Oct 2015	842 ± 34 p=0.25	703 ± 22 p=0.44	553 ± 15 p=0.38	445 ± 25 p=0.70	3.48 ± 0.038 p=0.91	2.71 ± 0.027 ***p=0.03***	2.21 ± 0.036 p=0.18	1.89 ± 0.050 p=0.59
Nov 2015	---	710 ± 25 p=0.34	545 ± 21 p=0.80	454 ± 17 p=0.25	---	2.76 ± 0.029 p=0.90	2.24 ± 0.049 p=0.72	1.84 ± 0.034 p=0.53
Dec 2015	---	---	565 ± 23 p=0.28	457 ± 22 p=0.34	---	---	2.34 ± 0.054 p=0.15	1.91 ± 0.045 p=0.33
Jan 2016	---	---	---	458 ± 25 p= 0.37	---	---	---	1.96 ± 0.050 p=0.05
Total sample	803 ± 7	686 ± 5	540 ± 5	435 ± 5	3.48 ± 0.008	2.77 ± 0.006	2.26 ± 0.011	1.86 ± 0.011

[a] P-values in bold italics are those for growth velocities that were significantly lower (p<0.05) than the overall sample mean
[b] Mean ± SE

4.6 Discussion

The aim of this Chapter was to describe patterns of attained size and rates of growth in infants 0-6 months of age in an agrarian population in rural India. We observed that mean attained size at almost every age between birth and six months was below -1 SD of the MGRS reference, and that the prevalence of undernutrition as estimated by several different anthropometric indicators was high at birth and remained high through six months of infant age. This study provides new information about growth by age and by month of year in a unique study context where irrigated agricultural practices are pervasive.

In our sample, we observed that LAZ, WAZ and WLZ remained fairly constant between one and six months of infant age, as did the prevalences of stunting wasting and underweight. There were more substantial changes observed for these indicators between birth and one month of infant age, especially for the prevalence of wasting. This may have been an artifact if the sample of births that we captured represented a select group of infants (**Chapter 3**). Similar to findings from the present study, a longitudinal study conducted in MINIMat, Bangladesh, showed that WAZ was fairly constant between one and six months of age (approximately 1.5 Z-scores below the MGRS sample median). In contrast, however, LAZ and WLZ followed slightly different patterns with age [154]. Compare to our sample, in MINIMat, mean LAZ showed a slightly greater decline (about -1 Z-scores at one month of age to around -1.5 Z-scores at six months of age relative to the MGRS sample median). In contrast, mean WLZ were relatively higher in the MINIMat sample (greater than the MGRS median at one month of age and about -0.2 Z-scores at six months of age relative to the MGRS sample). The prevalences of stunting and wasting, however, also remained relatively constant (between 30 and 40% underweight and between 25 and 30% stunted) and comparable to the prevalences observed in the present study.

The authors of the study conducted in MINIMat did not report the prevalence of wasting, but based on a comparison of mean WLZ, one would expect the prevalence of wasting to be higher in our sample [154]. The limited changes in nutritional status between one and six months of infant age could suggest a protective effect of persistent breastfeeding on nutritional status during the first six months of life. It is also possible that prenatal factors could play a relatively more important role than postnatal factors in early postnatal growth. Previously published research suggests that a high proportion of early growth faltering is attributable to prenatal factors, but likely varies across populations [22, 155, 156]. The relative influence of pre- and postnatal factors on growth in our sample is not fully understood and will be discussed in Chapter 5.

In the present study, we observed very high prevalences of undernutrition during the first six-month of life. At all ages between one and six months of age, nearly 30%, 40%, and 18% of our sample were stunted, underweight and wasted, respectively. The high proportion of our sample defined as undernourished by these various indicators underscores that undernutrition during early life is a public health concern. Recent analyses of undernutrition relative to the MGRS standard in infants less than six months of age in the National Family Health Survey-3 (NFHS-3) in India revealed nationwide prevalence estimates of stunting, wasting and underweight of 20.4% 30.6% and 29.6%, respectively [12]. Similar analyses of District Health Survey (DHS) data revealed estimates of wasting to be over 30% in infants less than six months of age throughout India [13]. In our sample, the prevalences of stunting and underweight were about 7-10 percentage points higher, while for wasting, the prevalence was close to ten percentage points lower. In a sample of Bangladeshi infants, de Onis and colleagues showed a higher prevalence of wasting in infants 6-11 months of age as compared to infants 0-5 months of age [9]. In contrast, Patwari, Kumar and Beard, reported higher prevalence estimates of undernutrition in infants less than six months of age, relative to infants 6-60 months of age in the NFHS-3 data [12]. Although outside the scope of the present dissertation, the prevalence of undernutrition in our sample of infants less than six months of age should be compared to the prevalence of undernutrition in nine and 12 month old infants from the same population to determine whether the observed trends persists.

A major feature of the current study is that we followed a cohort of children throughout the first six months of life and analyzed rates of growth from these longitudinal data. For both males and females in our sample, the rate of growth in weight and length was at, or slightly above -1 SD of the MGRS reference in the 0-3 and 1-4 month intervals, and below -1 SD of the MGRS reference in the 2-5 and 3-6 month intervals. This reflects some deceleration in growth in our sample in the second part of the 0-6 month growth interval, which is consistent with findings from other longitudinal growth studies of this age group [157]. Relative to the overall sample mean rate of weight gain, we observed no significant differences in the rate of weight gain in any month that started a three-month growth interval. The exception was a marginally significant difference observed when the 3-6 month growth interval began in March 2015 (31 g/mo less than the overall mean; p=0.067).

According to other published literature from South Asia, weight velocity varies throughout the year more than we observed in the present study [149-151, 158]. For infants less than 24 months of age in Bangladesh, for example, weight velocity tended to fall below an internal village reference during the rainy and pre-harvest periods (August-December) and then return to the level of the reference in January/February. The magnitude of these monthly differences in weight velocity was on the order of 3-4 fold [149]. Relative to the internal village reference, the authors also observed fluctuations in weight-for-length throughout the year. Weight-for-length began to decline in May, and then reached a nadir in September/October. The decline in WLZ observed in our cross-sectional sample was less apparent, but mean WLZ at almost every infant age tended to decline in July/August. In both settings, these months correspond to the monsoon period, a period of potentially high risk for poor health and nutritional status (**Chapter 2**). Compared to infants in the MGRS standard, this internal village reference likely represented infants who were raised under sub-optimal conditions (e.g. feeding and living conditions, etc.). In our sample, we also observed a tendency for lower WLZ to occur in infants that were born in March. The reasons for this may be due to a cohort effect. We did not, however, observe any strong evidence that differences existed between mothers and their infants born in March and mothers and their infants born in other months of the year. From preliminary analyses of our cross-sectional data, observed monthly differences in WLZ appear to be greater than WAZ. In young infants, weight-for-length may be a more sensitive indicator for detecting seasonal insults to nutritional status than weight for age. Seasonal variation in weight-for-length should be considered more thoroughly in longitudinal analyses of the present dataset, and in other datasets with available weight and length measurements for young infants.

Other previously published literature examining rates of growth in infants from rural areas of developing countries also tend to aggregate achieved growth for infants across a much wider age interval than in the present study and/or exclude infants 0-6 months of age. Therefore, the opportunity for direct comparison with our results is limited [97, 98, 152]. In one longitudinal study in Malawi, however, WAZ and LAZ increments (based on the older NCHS reference) for infants 0-6 months of age also declined most rapidly during the monsoon season. The authors also reported that WLZ increments were more variable month to month than other indicators of undernutrition [159].

One reason why we do not see greater monthly differences in rate of weight growth in three-month growth intervals possibly results from the labile nature of this measure. In our sample, the coefficients of variation for rates of weight growth tend to be larger than those for length growth, providing some limited support for this hypothesis (**Table 4.5**). It is also possible that the stresses affecting weight and length growth are governed by different biological mechanisms [85]. For example, if factors that affect weight growth are more variable from month to month, any potential association between month of year and rate of weight growth may have been difficult to detect over three-months, if it existed. Children less than six months of age may also be afforded some relative protection from seasonal stress due to protection via the mother (e.g. from breastfeeding) [97, 98, 152].

For rate of length velocity, a more expected pattern emerged. In general, across the four- three-month growth intervals, infants who were growing between January and June 2015 tended to have rates of length gain that were at or above the overall sample mean rate of length gain. Infants that were growing between approximately August and October 2015 tended to have rates of length growth that were below the overall sample mean length velocity. The most consistent trend occurred in the 1-4 month growth interval. Infants who began the 1-4 month period of growth in August, September, or October 2015 had rates of length growth that were 0.06-0.08 cm/month (0.18-0.24 cm over the three-month growth interval) less than the overall sample mean rate of length growth. A three-month period of growth that began between August and October 2015 corresponded to growth that occurred between approximately August and December 2015. This period coincided with the rainy pre-harvest period (July-September), followed by the rice harvest (October/November). In this setting, these months coincide with high agricultural labor demands, and potentially increased food insecurity, if household supplies of wheat were depleted before the rice harvest. The monthly differences observed for length velocity in Bangladesh were less than for weight velocity, and decreased in the period following the greatest decrease in weight velocity. In contrast to our observations, the mean percentage of their internal village reference for length was significantly lower between December and April, the post-harvest period in this Bangladesh [96]. It is possible that this difference is a reflection of divergent underlying agricultural systems, resulting in distinct patterns of risk factors for poor postnatal growth throughout the year. Compared to the other three-month growth intervals we examined, rate of length growth in the 1-4 month growth interval appeared to be more sensitive to exposure to the month of the year starting the interval.

Some previous studies have shown a lagged effect of weight growth on subsequent length growth [85]. Based on observed mean monthly values, however, we did not observe any apparent lag in the timing of peak mean rate of weight and length growth throughout the year (**Table 4.6; Table 4.7**). This phenomenon has been reported in some, but not all, previously published studies [85, 149, 151]. To investigate whether rate of growth in weight and length were associated in our sample, we conducted simple univariate analyses between rate of weight and rate of length growth within each three-month interval. We found that unit increases in rate of weight gain were significantly positivity associated with rates of length gain in each of the four- three-month intervals of the growth ($p<0.01$ for 0-3, 2-5 and 3-6 month growth intervals and $p=0.004$ for 1-4 month growth interval). Furthermore, in the two non-overlapping intervals (0-3 and 3-6 months), we found that rate of weight change in the 0-3 month interval was positively associated with rate length change in the 3-6 month interval ($p=0.002$), and reduced odds of stunting at six months of infant age ($p<0.01$). These highly significant associations remained after controlling for rate of length growth in the 0-3 month interval as a potentially confounding variable. These observations beg the question of whether there are underlying relationships between rates of weight and length gain in our sample that may help explain, in part, the high prevalence of early child stunting in Shivgarh and elsewhere in South Asia. This question should be explored in other longitudinal datasets that can examine shorter intervals of growth and growth variability.

This study has the advantage that it was a prospective design in which pregnant women were recruited continuously over a 15-month period. Our findings provide new insights as to the patterns of attained size and rates of growth by age and by month of year in an understudied age group from a novel study context. Compared to estimating growth rates in an age interval by computing a difference in two measures of attained size, our methodological approach to estimating growth rates using random slopes and intercepts models is advantageous because it utilizes all of the available information during the growth interval. In addition, this approach allowed us to minimize loss of sample size because the two measurements required to estimate a slope within an interval were not constrained to any specific time within the interval. By estimating slopes in three-month intervals, we were able to capture nearly 80% of the sample of infants who were measured during their first six months of life. Of the 383 valid growth measures taken at the birth visit (measured within 14 days of birth), we were able to estimate rates of growth for approximately 89%, 87%, 83% and 75% of these infants in the 0-3, 1-4, 2-5 and 3-6 months of age intervals, respectively, which speaks to the high representativeness of our longitudinal cohorts.

After the birth visit, permanent loss to follow-up was relatively low, but the proportions of temporary refusals and unavailability of the mother were relatively high (**Figure 2.4**). Teams of enumerators were often not able to revisit households within 14 days of the infant's monthly birthday to measure the infant. This was likely due to logistical challenges (e.g. poor roads, reduced staffing, mothers busy with other tasks at time of visit, etc.), as opposed to other reasons that may have introduced potential sources of bias (e.g. enumerators not re-visiting more remote households). If bias had occured, however, one might expect that infants from more remote households would have poorer nutritional status due to factors such as lower socio-economic status, poorer access to health services, etc. Under this scenario, it is more likely that our sample estimates of rate of growth were an overestimate, rather than an underestimate.

While our sample of infants that make up the various longitudinal age group samples may be representative of the entire birth sample, it does not assure a lack of bias in sampling the birth cohort. In some months of the year, we did not obtain the targeted universal sample of births. Consequently, some monthly birth cohorts had sample sizes that were relatively small (n=11-32). In the 1-4 month growth interval, mean rate of length growth was significantly lower than the overall sample mean rate of length growth when growth began between August and October 2015. Two out of these three months (August and October 2015, or the July and September 2015 birth cohorts, respectively), represent birth cohorts that had relatively small sample sizes (n=12 and 16, respectively). We did not, however, observe any strong evidence of differential selection bias associated with small birth cohorts as discussed in Chapter 3. We cannot, however, fully exclude the possibility that these infants represented a select group.

In conclusion, during the first six months of life, infants in our sample had substantial deficits in both attained size and rates of growth relative to the MGRS standard population. Prevalence estimates of stunting, wasting and underweight in early life in our sample were extremely high and represent a significant public health concern. We observed significant monthly differences in length, but not weight velocity. The reasons for these observations should be explored in other datasets with shorter intervals of growth to address the potentially more labile nature of weight growth. Of the various three-month growth intervals we explored, length velocity in the 1-4 month growth interval appeared to be more sensitive to exposure to month of the year starting the interval. The significant differences observed for length velocity in the 1-4 month growth interval relative to the overall sample mean length velocity were, however, relatively small, and unlikely to be of large public health importance. These deficits, however, could have cumulative effects on growth and development over the entire six-month period, and possibly into later infancy. The prevalences of undernutrition were high at birth and remained high, which suggests a strong influence of prenatal factors on postnatal size and rates of growth. The association between month of year and pre- and postnatal maternal and infant factors (e.g. size at birth, infant feeding, morbidly and food insecurity, etc.) and infant weight and length velocity in the 1-4 month interval of growth will be examined in Chapter 5.

Chapter 5

Aim 3: Association of time-independent maternal and infant factors, time-dependent infant postnatal and maternal postpartum characteristics and season with rates of weight and length growth from 1-4 months of age

Madan EM, Haas JD, Frongillo EA, Kumar V, Kumar A, Menon P

5.1 Abstract

Growth velocity, or rate of change in body size during a given time interval, provides important insights into growth processes. Changes in rate of growth may signal an adverse response to an environmental insult prior to an observed effect on attained size. Few published studies are available, however, to understand the predictors of rates of postnatal growth, especially in infants less than six months of age in low-resource populations. The objective of the present study was to examine the association of time-independent maternal and infant factors, time-dependent infant postnatal and maternal postpartum characteristics and season with rates of weight and length growth from 1-4 months of age. From August 2013-April 2015, a longitudinal study of infant growth was conducted in Shivgarh, Uttar Pradesh, India. Data on anthropometry and potential risk factors for poor postnatal growth were collected each month from birth to six months of infant age. Univariate and multivariable regression analyses were conducted for weight and length velocity considered separately as dependent variables. In multivariable regression analyses both maternal and infant prenatal (sex, newborn size, parity and maternal height), infant postnatal (exclusive breastfeeding) and maternal postpartum (morbidity and work in agriculture) factors were important determinants of rate of weight and length gain. Infant morbidity was negatively associated with rate of both weight and length gain, but only in un-vaccinated infants. Time spent in childcare negatively affected rate of length growth, but only during the higher-risk season. This study contributes new information from a

novel study setting to help identify potentially important modifiable risk factors for growth faltering during the first six months of life.

5.2 Introduction

Assessment of static measures of infant size (attained body size) can help to understand a child's current nutrition and health status, but cannot provide sufficient insight as to how the child arrived at a given size. On the other hand, growth velocity, or the rate of change in size over a given time interval, allows for the examination of growth processes. Patterns of growth velocity, and the ability for growth to respond in the short-term are hypothesized to serve as adaptive responses to the environment that contribute to survival [160-162]. For example, a deceleration in growth may be associated with an environmental insult such as infection. Once the insult is ameliorated, periods of more rapid growth, or even a return to a child's normal growth trajectory ("catch-up" growth) may occur [43]. Several studies report marked changes in incremental growth that occurred prior to any substantial reduction in attained size as the outcome [98, 99]. Therefore, compared to attained size, the examination of patterns of infant growth velocities can allow for the earlier detection of risk for poor health and nutritional status.

Previously published literature documents the important associations that may exist between various pre-and postnatal factors (e.g. size at birth, patterns of breastfeeding, season of the year, etc.) and risk of undernutrition in early life, most frequently examined with attained size [91, 96, 127, 163]. Poor growth in early life, especially during the first 1000 days (the period from conception to approximately two years of age), is associated with adverse health, cognitive and economic consequences later in life [28, 164]. In addition, in South Asia, undernutrition assessed by attained body size occurs earlier than previously thought. By six months of age estimates of stunting and wasting are alarmingly high, especially in India [9, 13]. This results in part from limitations in the use of growth references available before the 2006 Multicentre Growth Reference Study (MGRS) standard. Factors affecting rates of early child growth, especially for undernourished infants less than six months of age, however, are not well understood [10, 13]. A better understanding of changes in incremental growth during this vulnerable period of life will allow for the earlier detection of the process that leads to undernutrition, and thus the earlier initiation of interventions to prevent associated poor outcomes in infancy and later life.

Longitudinal studies of infants during the first six postnatal months of life that integrate frequent anthropometric measures with measures of a broad range of risk factors for poor health and nutritional status are relatively rare. The objective of the present study was to examine the association of time-independent maternal and infant factors, time-dependent infant postnatal and maternal postpartum characteristics and season with rates of weight and length growth from 1-4 months of age. Based on our conceptual framework (**Figure 1.3)**, we hypothesized that various fixed, time-independent infant and maternal characteristics (measured during the late third trimester of pregnancy) and time-dependent infant postnatal and maternal postpartum factors would be associated with rate of growth between one and four months of infant age.

5.3 Methods

5.3.1 Study design and sample

The methods applied to this study have been described in detail in Chapters 2-4. In brief, from August 2013 to April 2015, a longitudinal study of infant growth was conducted in nine selected villages in Shivgarh, Uttar Pradesh, India. Pregnant women were recruited in the late third trimester of pregnancy and mother-infant pairs were followed from birth until six month of infant age. At each visit, trained and standardized enumerators conducted in-depth interviews with mothers and collected maternal and child anthropometry. We examined growth velocity in four three-month age increments (0-3 mo, 1-4 mo, 2-5 mo, and 3-6 mo), as described in Chapter 4. Because of the non-linear nature of growth during the first six months of life, and the likely age specificity of many of the risk factors for poor growth (e.g. morbidity, feeding behaviors, etc.), a three-month period of observation for subsequent analyses was considered preferable to a longer interval (e.g. from 0-6 months of age). From these descriptive analyses, we determined that the 1-4 month growth interval was the most appropriate interval for subsequent analyses for several reasons. First, the 0-3-month age interval includes measures of newborn size. Compared to other intervals, this interval is thus potentially more reflective of prenatal, rather than postnatal influences on infant growth. Second, all growth intervals showed negative deviation from the MGRS standard median, but the 1-4 month age interval had a greater sample size compared to either the 2-5 month or 3-6 month age intervals. Lastly, the 1-4 month growth interval was the only interval observed to be sensitive to exposure to month of the year at the beginning of the interval (for length velocity only). This allowed for an analysis of mediation and modification of seasonal effects by possible other measured determinants of growth.

5.3.2. Measurements

Rate of infant weight and length growth were the outcome variables of interest. The collection and handling of anthropometric data were described in detail in Chapters 2-4. Variables reflecting both maternal and infant fixed characteristics (defined in this paper as time invariant characteristics), and time or age dependent postnatal factors were considered as potential determinants of rate of infant weight and length growth. Fixed infant characteristics considered were newborn size, sex, parity, and gestational age. Fixed maternal characteristics considered were height, village and socio-economic status. The collection of these data, and construction of the variables use in the analyses were described in detail in Chapter 3. The postnatal characteristics of the infant considered were clusters of months of year representing the beginning of the 1-4 month growth interval, morbidity, exclusive breastfeeding, vaccination and childcare. The postpartum, time/age dependent, characteristics of the mother considered were morbidity, food insecurity, diet diversity, agricultural work and weight change.

Data collected at the visits corresponding to two, three and four-months of infant age were considered the relevant data for growth velocity during the 1-4 month growth interval. The data collected at the visit corresponding to first-month of infant age were not considered relevant because the recall period reflected the period between birth and one month of infant age, and were therefore outside the interval of interest. Maternal postpartum and infant postnatal characteristics were collected at each monthly visit, with the exception of food insecurity and diet diversity. Food insecurity data were collected at the visits corresponding to two and four months of infant age, and diet diversity data were collected at the visit corresponding to three months of infant age (**Appendix A**). For data collected monthly, mother-infant pairs had the potential for up to three measurements during the interval. As a result of missing visits (most likely because of constraints in data collection under field conditions), data for all three possible visits were frequently not available. Of the 332 infants with a valid measure of either weight or length velocity in the 1-4 month growth interval, 36, 143, and 153 infants had data available for the visits corresponding to one-, two-, and three-months of infant age, respectively (for data collected monthly).

We examined cross-sectional, maternal postpartum and infant postnatal data by infant age to assess for time-variation. Cross-sectional rather than longitudinal data were used for this assessment because of within-child missing data. With the exception of exclusive breastfeeding, there was no evidence that any of the postnatal or postpartum data varied by infant age between two and four months. Therefore, to minimize bias associated with individual infants contributing a different number of measures (at different visits) during the interval, we averaged data (continuous and categorical) for postnatal variables, except exclusive breastfeeding, across all available visits between two and four months of infant age. Mean values for all variables were visually examined by weight and length velocity in two-way scatter plots and expressed as either continuous or categorical variables for use in subsequent analyses.

Season of growth

The month at the start of the 1-4 month growth interval was dichotomized as either "higher-risk" season (August-October 2015) or "lower risk" season (all other months). This classification was based on observations that infants who began the 1-4 month growth interval between August and October 2015 had rates of length growth that were significantly lower than the overall sample mean length velocity (**Chapter 5**).

Infant morbidity

Information about infant morbidity was collected by maternal recall of symptoms (cough, fever, diarrhea, vomiting, refusal to eat) during the previous seven days. Univariate analyses of the mean value of individual symptom between two and four months of infant age (range 0-1) with infant weight and length velocity were conducted. Only mean values for cough, fever and diarrhea were found to have important negative associations ($p<0.2$) with one or both growth velocity measures. Therefore, information regarding the occurrence of these three individual symptoms and the number of total days the symptom occurred (1-7 days) was used to construct a morbidity score for each child at all available visits during the interval. Each symptom was multiplied by the number of days, and then summed for each individual child (range 0-21). A within child mean of morbidity scores at all available visits during the interval was calculated. An individual level mean morbidity score was considered as a continuous variable in subsequent analyses (**Table 5.1**).

Exclusive breastfeeding

Infant feeding data were collected each month by maternal recall of all foods (liquid and solid) given to the infant in the previous 24-hours. Infants were classified as either exclusively breastfed, or not, at every available visit based on the World Health Organization (WHO) definition of exclusive breastfeeding (breastmilk and no other liquid or solids) [165]. A mean value of exclusive breastfeeding to represent the entire 1-4 months growth interval was considered inappropriate because the odds of exclusive breastfeeding in our sample was decreased between two and four month of infant age. Therefore, infants reported as exclusively breastfed at four months of age, were assumed to have been exclusively breastfed for the entire interval, and vice versa. Twenty-eight infants were missing data for exclusive breastfeeding at four months of age, but had data available at three months of age. To maximize the amount of available data, we expanded our criteria to include the assumption that the breastfeeding status of these 28 infants at three months of age was also likely to reflect their breastfeeding status for the entire interval. We checked this assumption by comparing models that either included or excluded these 28 infants and observed negligible differences in model parameters. Exclusive breastfeeding status was considered as a dichotomous categorical variable in subsequent analyses (**Table 5.1**).

Table 5.1 Summary of maternal postpartum and infant postnatal variables used in analyses of infant weight and length velocity in the 1-4 month growth interval

Variable (units)	Description of variable	Range of values
Infant prenatal		
Sex	Dichotomous (male=0; female=1)	0,1
Gestational age, wk	Date of birth minus date of LMP	37.0-42.9
Parity	Dichotomous (multiparous=0; primiparous)	0,1
Newborn weight, g	Infant weight measured within seven days of birth	1.45 -4.02
Newborn length, cm	Infant length measured within seven days of birth	41.5 -53.6
Maternal prenatal		
Height, cm	Maternal height measured during third trimester of pregnancy	138.8- 164.6
Socio-economic status	Three-level categorical (lower tertile (lowest class)=1, middle tertile=2; higher tertile=3)	1-3
Village	Eight dummy variables for nine villages	0,1
Infant postnatal		
Season beginning growth interval (mo)	Dichotomous (all other months=0; Aug-Oct 2015=1))	0,1
Morbidity	Morbidity score (0=no morbidity)	0 -21
Exclusive Breastfeeding	Dichotomous (not exclusively breastfed for entire interval=0; exclusively breastfed for entire interval=1)	0,1
Childcare, min/d	Mean time spent in childcare	135-690
Vaccination	Dichotomous (received no age appropriate vaccines during interval=0; received any age-appropriate vaccines during interval=1)	0,1
Maternal postpartum		
Morbidity	Morbidity Score (0=no morbidity)	0 -24
Work in agriculture	Three-level categorical (lower tertile (least work)=1, middle tertile=2; higher tertile =3)	1-3
Food insecurity	Three-level categorical (Never food insecure during interval=1, Sometimes food insecure during interval=2, always food insecure during interval=3)	1-3
Diet diversity	Dichotomous (consumed < 5 food groups=0; consumed $\geq$ 5 food groups=1)	0,1
Weight velocity, kg/mo	Change in maternal weight between 1 and 4 months of infant age	-3.3- 2.6

Infant care

Infant-care data were derived from a 24-hour activity recall questionnaire administered to mothers at each visit [166]. Care was defined as the number of minutes that the mother spent in direct childcare activities (e.g. feeding, bathing, etc.) during the previous 24-hours. A within child mean of minutes spent in childcare was computed from all available visits in the interval. Childcare was considered as a continuous variable in subsequent analyses (**Table 5.1)**.

Infant vaccination

Information regarding receipt of age-appropriate vaccines[9] during the past 30 days was collected via maternal recall, and examination of the government health card (if available) each month. A child that received any age-appropriate vaccines at a visit was considered vaccinated. The dichotomous vaccination variable was averaged within each child across all available visits between two and four months of age (range 0-1). Vaccination was considered as a dichotomous categorical variable in subsequent analyses (**Table 5.1)**.

Maternal morbidity

Maternal morbidity was collected by self-report of symptoms during the previous seven days. Based on univariate analyses, however, none of the individual symptoms (cough, fever, diarrhea, injury, headache) were associated with either infant weight or length velocity ($p<0.2$). Therefore, under the assumption that a global indicator of health, rather than the occurrence of individual symptoms, would be a more meaningful variable, a morbidity score was constructed based on the available data for all six reported symptoms (cough, fever, vomiting, diarrhea, headache and injury). The morbidity score (0-35) was constructed based on occurrence and duration of

[9] Between two and four months of infant age, the Indian government recommends vaccination against polio, diphtheria, pertussis (whooping cough), and tetanus and tuberculosis (**Appendix A**).

symptoms as previously described for infant morbidity data. Individual mean maternal morbidity scores between two and four months of infant age were considered as a continuous variable in subsequent analyses (**Table 5.1)**.

Maternal work in agriculture

Similar to the previously described childcare data, data on maternal work in agriculture were collected each month via maternal report of activities in the past 24-hours. Maternal work in agriculture was defined as the total number of minutes the mother spent working in agriculture. The mean number of minutes spent in agriculture between two and four months of infant age was calculated for each mother. Mean values were then divided into tertiles for use in subsequent analyses (**Table 5.1)**.

Food insecurity

The Household Food Insecurity Access Scale (HFIAS) was administered to mothers at two separate visits between two and four months of infant age [137]. An HFIAS score was calculated at each visit (range 0-14), and women were classified as either food insecure or food secure, as described in Chapter 3. The mean of continuous (range 0-14), and dichotomous food insecurity measures (range 0-1) was calculated for each mother. Mean values of the dichotomous food insecurity measure were categorized into one of three categories (0, 0.5, or 1) for subsequent analyses (**Table 5.1)**.

Maternal diet diversity

Data on food items consumed by the mother in the past 24-hours were collected by maternal recall just once between two and four months of infant age. Reported food items were classified into one of 10 pre-coded food group categories according to the minimum diet diversity guide (**Appendix A**) [167]. The number of food groups was summed to create a diet diversity score (range 0-10), and women were classified as having consumed greater than or equal to five food groups, or less than five food groups for use in subsequent analyses (cut-off defined by minimum diet diversity guide) [167](**Table 5.1)**.

Maternal weight velocity

Maternal weight (kg) was collected at each visit between one and four months of infant age. Change in maternal weight during the interval was estimated using the same methodology (empirical Bayes estimates of slopes of size by age) used to estimate infant weight and length changes as described in Chapter 3 (**Table 5.1)**. Individual weight change during the interval was considered as a continuous variable in subsequent analyses.

5.3.3 Statistical approach

Characteristics of the study population were summarized as mean ± SD for continuous variables or counts with percentages for categorical variables. To examine whether the observed negative association between certain months of the year and rate of length growth in the 1-4 month interval of growth was mediated by hypothesized maternal factors (food insecurity, diet diversity, morbidity, work in agriculture, weight velocity) and infant factors (breastfeeding, morbidity, childcare, vaccination), we tested for mediation using VanderWeele's method [168] (**Appendix D**). Univariate regression analyses were conducted separately for weight and length velocity during the 1-4 month interval as dependent variables. Any univariate association with a p-value < 0.2 was considered as potentially important. To allow for exploratory screening of possible biologically plausible interactions, however, all variables were considered in subsequent multivariable regression models, regardless of univariate p-value. Multivariable regression analyses were conducted separately for weight and length velocity during the 1-4 month interval. Missing data for independent variables were assumed to be missing at random (MAR), and were thus handled using a structural equation modeling procedure that implemented full information maximum likelihood [139].

We added independent variables to multivariable regression models according to our conceptual framework **(Figure 1.3)**. First, infant and maternal fixed, time-independent characteristics (infant sex, early neonatal size, parity, gestational age, maternal height, socio-economic status and village) and season starting the growth interval were added to models. Second infant postnatal determinants (morbidity, breastfeeding, vaccination, care) were added, followed by maternal postpartum determinants (morbidity, food security, diet diversity, agricultural work, weight change). Finally, interaction terms were added to models. We tested possible biologically plausible two- and three- way interactions 1) between season starting the growth interval and maternal and infant fixed characteristics and postnatal determinants), 2) between infant postnatal variables and 3) between maternal postpartum and infant postnatal variables. In multivariable regression models, we observed evidence of collinearly between village and SES. We chose to include only village in final models because village was believed to capture observed SES differences as well as other potentially unobserved characteristics between villages. All analyses were conducted using Stata version 13 (StataCorps, TX). Statistical significance was defined as $p<0.05$ for main effects, and $p<0.1$ for interactions.

5.4 Results

The proportion of male and female infants with valid measures of either weight or length velocity were approximately equal (47.3% female) (**Table 5.2**). The proportion of infants who began growth in the high-risk season (17.5%) was lower than would be expected (21.4%) if an equal number of infants had been born in each month (**Chapter 3**). Approximately one third of the sample (33.2%) was exclusively breastfed for the entire interval. The low sample mean food insecurity score (1.06 ± 1.81) and nearly 60.0% of mothers who were never classified as food insecure during the 1-4 month growth interval suggests a relatively food-secure sample. The mean number of minutes per day spent in agricultural work (30.5 ± 51.9) and childcare (370 ± 83) represent approximately 2.0% and 25.0% of a total day (1440 minutes), respectively. The low proportion of time spent in agricultural activities suggests a relatively low level of participation in agricultural labor.

In univariate analyses of length velocity as the dependent variable, the important ($p<0.2$) infant and maternal time invariant variables were infant sex, newborn length and weight, primiparity, gestational age, maternal height, SES, and village (**Table 5.3**). The important maternal and infant time/age dependent variables were season at beginning of interval, infant morbidity, vaccination, diet diversity, work in agriculture and maternal weight velocity. In univariate analyses of weight velocity as the dependent variable, the important variables were somewhat different. Important infant and maternal prenatal variables were sex, newborn weight and length, maternal height, SES and village. Important infant postnatal and maternal postpartum variables were exclusive breastfeeding, vaccination, childcare, and work in agriculture.

We observed no evidence for mediation of the relationship between month of year and rate of length growth in the 1-4 month interval by maternal and infant risk factors, considered independently (**Appendix D**). Multivariable regression analyses of length velocity as the dependent variable revealed that female infants grew 0.39 cm/month slower in length that male infants (**Table 5.4 Model 4**). Unit increases in newborn recumbent length and maternal height, in contrast, were associated with 0.022 cm/month ($p<0.001$), and 0.004 cm/month ($p=0.005$) greater infant length gain, respectively. Compared to mothers who spent the least amount of time in agricultural work (lower tertile), growth in length was significantly lower only in the group of mothers who spent an intermediate amount of time (middle tertile) ($p=0.027$) Childcare was significantly negatively associated with length velocity when growth began in the higher-risk season, but not when growth began in the lower-risk season (interaction p=0.019) (**Figure 5.1**). Infant morbidity was significantly negatively associated with length velocity in infants that did not receive any age appropriate vaccines during the interval, but not in infants that received vaccines (p=0.001 for interaction) (**Figure 5.2**).

Table 5.2 Characteristics of mothers and infants in Shivgarh (n=332)

Variables	Mean ± SD	N (%)
Infant and maternal fixed time invariant characteristics		
Sex		
Female	---	157 (47.3)
Early neonatal size (n=203)		---
Length, cm	48.0 ± 2.3	---
Weight, kg	2.7 ± 0.5	---
Parity (n=278)	2.7 ± 1.9	---
Primiparious	---	69 (27.7)
	39.5 ±1.4	
Gestational age, wk (n=231)		
	149.9 ± 5.2	---
Height, cm (n=249)		
	---	---
Socio-economic status (n=259)		
Lower tertile	---	88 (34.0)
Middle tertile	---	84 (32.4)
Upper tertile	---	87 (33.6)
Village	---	
1	---	39 (11.8)
2	---	38 (11.5)
3	---	36 (10.8)
4	---	69 (20.8)
5	---	44 (13.3)
6	---	15 (4.5)
7	---	20 (6.0)
8	---	44 (13.3)
9	---	27 (8.1)
Infant time variant postnatal determinants		
Season		
High risk (August-October 2015)	---	58 (17.5)
Low risk (all other months)	---	274 (82.5)
Morbidity score	6.8 ± 4.8	---
	---	---
Breastfeeding (n=319)		
Exclusively breastfed for entire interval	---	106 (33.2)
Not exclusively breastfed for entire interval	---	213 (66.8)
	---	---
Vaccinations (n=329)		
Received no age appropriate vaccines	---	65 (19.8)
Received any age appropriate vaccines	---	264 (80.2)
	370 ± 83	---
Childcare, min/d (n=331)		

Table 5.2 (continued)

Maternal time variant postnatal determinants		
Morbidity score	3.0 ± 3.8	
Food insecurity score	1.06 ± 1.81	
Never food insecure during interval	---	190 (59.8)
Some food insecure during interval	---	49 (15.4)
Always food insecure during interval	---	79 (24.8)
	3.29 ± 1.0	---
Diet diversity (n=285)		
Consumed <5 food categories	---	258 (90.5)
Consumed ≥5 food categories	---	27 (9.5)
	30.5 ± 51.9	---
Agricultural work, min/d		
Lower tertile	---	193 (58.1)
Middle tertile	---	46 (13.9)
Upper tertile	---	93 (28.0)
Weight velocity, kg/mo	-0.16 ± 0.66	---

Table 5.3 Results of univariate analyses of length and weight velocity of infants in the 1-4 month growth interval with prenatal characteristics and maternal postpartum and infant postnatal variables

Variables	Length Velocity cm/mo (n=330)[a]	Weight Velocity g/mo (n=332)[a]
Infant and maternal fixed characteristics		
Sex		
Female	-0.015± 0.012	-55± 10
Male	p=0.20	p<0.001
	Ref	Ref
Newborn size		
Length, cm	-0.018 ± 0.003	16 ± 3
	p<0.001	p<0.001
Weight, g	-.079 ± 0.015	66 ± 12
	p<0.001	p<0.001
Parity		
Multiparous	Ref	Ref
Primiparious	0.043 ± 0.015	5 ± 13
	p=0.005	p=0.68
Gestational age, wk (n=231)	-0.010 ± 0.005	-0.2 ± 4
	p=0.080	p=0.96
Height, cm (n=249)	0.002± 0.001	3 ± 1.1
	p=0.18	p=0.009
Socio-economic status (n=259)		
Lower tertile	Ref	Ref
Middle tertile	-0.029 ± 0.017	-21 ± 14
	p=0.080	p=0.134
Upper tertile	-0.025 ± 0.017	-17± 14
	p=0.13	p=0.20
Village		
1	Ref	Ref
2	0.028 ± 0.025	-31 ± 20
	p=0.27	p=0.13
3	-0.002 ± 0.025	-43 ± 21
	p=0.95	p=0.036
4	-0.007 ± 0.022	-10 ± 18
	p=0.76	p=0.57
5	0.021 ± 0.024	-20 ± 20
	p=0.38	p=0.31
6	0.057 ± 0.033	-59 ± 27
	p=0.08	p=0.030
7	0.014 ± 0.030	-50 ± 25
	p=0.63	p=0.040
8	-0.006 ± 0.024	-13 ± 20
	p=0.80	p=0.51
9	-0.010 ± 0.028	-61 ± 22
	p=0.73	p=0.006

Table 5.3 (continued)

Infant postnatal determinants		
Season beginning growth interval		
Low risk (Aug-Oct 2015)	0.077 ± 0.015 p<0.001	-6 ± 13 p=0.63
High risk (All other months)	Ref	Ref
Morbidity score	-0.002 ± 0.001 p=0.061	0.2 ± 1 p=0.83
Breastfeeding	---	---
Exclusively breastfed for entire interval	-0.002 ± 0 .013 p= 0.894	17.05 ± 10.72 p=0.112
Not exclusively breastfed for entire interval	Ref	Ref
Vaccinations		
Received no age appropriate vaccines	Ref	Ref
Received any age appropriate vaccines	0.020 ± 0.015 p=0.20	17± 13 p=0.18
Childcare, min/d	-0.00001 ± 0.00007 p=0.88	.01 ± 0.1 p=0.059
Maternal postpartum determinants		
Morbidity score	-0.001 ± 0.002 p=0.41	-1 ± 1 p=0.34
Food insecure		
Never during interval	Ref	Ref
Sometimes during interval	-0.022 ± 0.018 p=0.21	-13 ± 15 p=0.39
Always during interval	0.005 ± 0.015 p=0.72	7 ± 12 p=0.59
Diet diversity	---	---
Consumed <5 food categories	0.031 ± 0.022 p=0.16	19 ± 18 p=0.30
Consumed ≥5 food categories	Ref	Ref
Agricultural work	---	---
Upper tertile	-0.022 ± 0.014 p=0.115	-26 ± 11 p=0.022
Middle tertile	-0.046 ± 0.018 p=0.011	12 ± 15 p=0.401
Lower tertile	Ref	Ref
Weight velocity, kg/mo	0.012 ± 0.009 p=0.20	-4 ± 8 p=0.60

[a] Coefficient ± SE

Table 5.4 Association of time-independent fixed, time invariant[a] maternal and infant characteristics and time-dependent infant postnatal[b] and maternal postpartum characteristics with length velocity (cm/mo) in the 1-4 month growth interval using structural equation modeling

Variables	Model 1[d,e] (n=330)	Model 2 [d,f] (n=330)	Model 3 [d,g] (n=330)	Model 4[d,h] (n=330)
Female	-0.032 ± 0.012 p=0.006	-0.034 ± 0.012 p=0.004	-0.034 ± 0.012 p=0.004	-0.039 ± 0.011 p=0.001
Male	Ref	Ref	Ref	Ref
Newborn length, cm	-0.020 ± 0.003 p<0.001	-0.021 ± 0.003 p<0.001	-0.020 ± 0.003 p<0.001	-0.022 ± 0.003 p<0.001
Starts growth interval in higher risk season (Aug-Oct 2015)	-0.060 ± 0.016 p<0.001	-0.061± 0.016 p<0.001	-0.064 ± 0.016 p<0.001	0.204 ± 0.115 p=0.076
Starts growth in lower risk season (all other months)	Ref	Ref	Ref	Ref
Maternal height, cm	0.004 ± 0.001 p=0.001	0.004± 0.001 p=0.003	0.004± 0.001 p=0.003	0.004 ± 0.001 p=0.005
Exclusively breastfed	---	0.019 ± 0.012 p=0.115	0.019± 0.012 p=0.128	0.022 ± 0.012 p= 0.065
Not exclusively breastfed	---	Ref	Ref	Ref
Received any vaccines	---	0.006 ± 0.015 p=0.680	0.011 ± 0.015 p=0.469	-0.061 ± 0.026 p=0.020
Received no vaccines	---	Ref	Ref	Ref
Child morbidity	---	-0.001± 0.001 p=0.27	-0.001± 0.001 p=0.28	-0.012 ± 0.003 p<0.001
Childcare, min/d	---	0.00003 ± 0.00 p=0.691	-3.70e-06 ± 0.00 p=0.96	0.00004 ± 0.00 p=0.57
Higher agriculture tertile	---	---	-0.018 ± 0.013 p=0.17	-0.019 ± 0.013 p=0.17
Middle agriculture tertile	---	---	-0.038± 0.017 p= 0.027	-0.037 ± 0.017 p=0.027
Lower agriculture tertile	---	---	Ref	Ref
Maternal morbidity	---	---	0.002 ± 0.002 p=0.27	0.003 ± 0.002 p=0.081
High risk season * childcare	---	---	---	-0.0007 ± 0.0003 p=0.019
Child morbidity* vaccination	---	---	---	0.012 ± 0.003 p=0.001
R^2	0.25	0.25	0.27	0.32

[a] Maternal and infant prenatal variables include maternal height, parity, infant sex, gestational age and early neonatal length
[b] Maternal postpartum variables include morbidity, food security, diet diversity, weight velocity, and agricultural work; Infant postnatal variables include month starting the growth interval, morbidity, breastfeeding, vaccination and childcare
[c]All models control for village as a fixed effect
[d] Mean ± SE
[e]Model 1 considers maternal and infant prenatal variables, season starting growth interval and interactions; variables with p >0.1 were not included in final models
[f] Model 2 adds infant postnatal variables; variables with p >0.1 were not included in final models
[g] Model 3 adds maternal postpartum variables; variables with p >0.1 were not included in final models
[h] Model 4 adds interactions; variables with p >0.1 were not included in final models

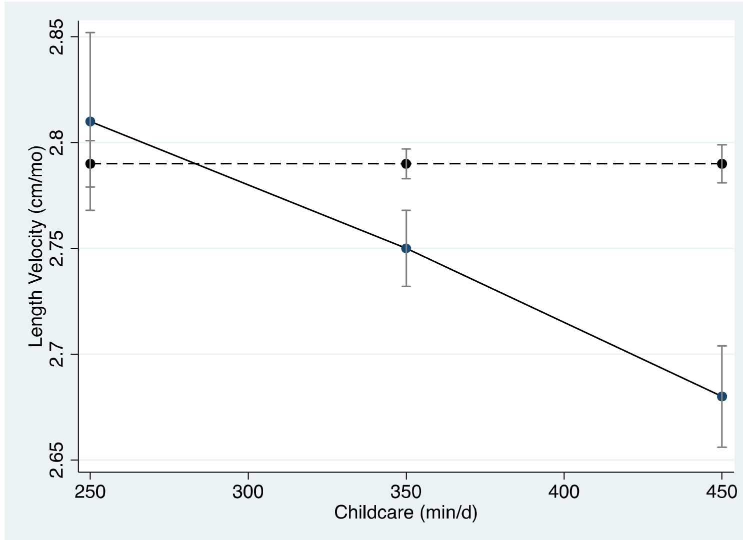


Figure 5.1 Relationship between childcare (min/day) and rate of infant length growth (cm/month) depending on time of year at start of the growth interval (interaction p=0.001) (dashed line represents “lower-risk” season; solid line represents “higher-risk” season)

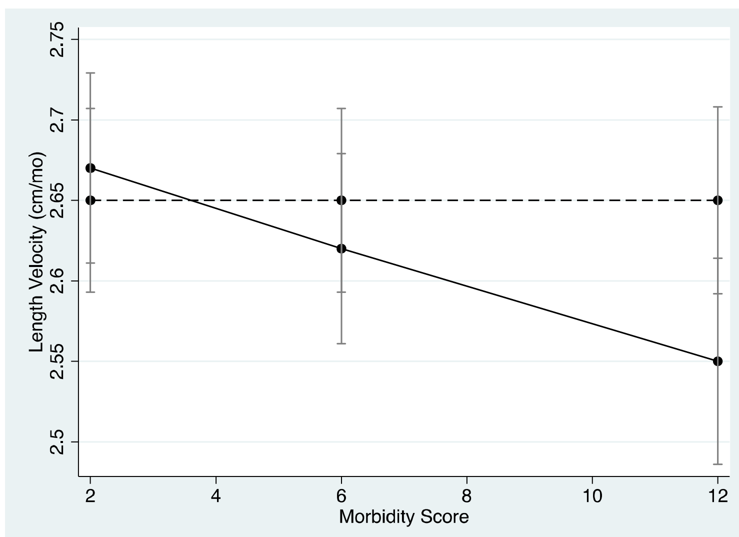


Figure 5.2 Relationship between morbidity score and rate of infant length growth (cm/mo) depending on infant vaccination status (interaction p=0.019) (dashed line represents vaccinated infants; solid line represents unvaccinated infants)

Multivariable regression analyses of weight velocity as the dependent variable indicate that female sex and primiparity were associated with 46 g/month ($p<0.001$) lower weight gain, and 22 g/month ($p=0.074$) higher weight gain, respectively (**Table 5.5 Model 4**). Each kg increase in newborn weight was associated with a 69 g/mo ($p<0.001$) higher infant weight gain. Compared to mothers spending the least amount of time in agricultural work (lower tertile), growth in weight was marginally significantly lower only in the group of mothers who spent the most amount of time (higher tertile) ($p=0.108$). Similar to models of length velocity as the dependent variable, infant morbidity was significantly negatively associated with weight gain in infants that did not receive any age appropriate vaccines during the interval, but not in infants that received vaccines (interaction $p=0.072$) (**Figure 5.3**).

Table 5.5 Association of time-independent fixed[a] maternal and infant variables and time-dependent infant postnatal[b] and maternal postpartum variables with weight velocity in the 1-4 month growth interval (g/mo) using structural equation modeling[c]

Independent Variables	Model 1[d,e] (n=332)	Model 2[d,f] (n=332)	Model 3[d,g] (n=332)	Model 4[d,h] (n=332)
Female	-45 ± 9 p<0.001	-46 ± 9 p<0.001	-44 ± 9 p<0.001	-46 ± 9 p<0.001
Male	Ref	Ref	Ref	Ref
Newborn weight, kg	71± 12 p<0.001	70 ± 12 p<0.001	70 ± 12 p<0.001	69 ± 12 p<0.001
Primiparous	25 ± 12 p=0.041	4 ± 12 p=0.050	23 ± 13 p=0.074	22 ± 13 p=0.081
Multiparous	Ref	Ref	Ref	Ref
Exclusively breastfed	---	16 ± 10 p=0.097	15.44 ± 10 p=0.119	17 ± 10 p=0.079
Not exclusively breastfed	---	Ref	Ref	Ref
Received any vaccines	---	10 ± 12 p=0.39	11 ± 12 p=0.35	-20 ± 21 p=0.333
Received no vaccines	---	Ref	Ref	Ref
Child morbidity	---	-2 ± 1 p=0.075	-2 ± 1 p=0.056	-6 ± 3 p=0.016
Higher agriculture tertile	---	---	-17 ± 11 p= 0.121	-17 ± 11 p=0.108
Middle agriculture tertile	---	---	12 ± 14 p=0.41	11 ± 14 p=0.41
Lower agriculture tertile	---	---	Ref	Ref
Morbidity*vaccination	---	---	---	5 ± 3 p=0.072
R^2	0.26	0.28	0.29	0.30

[a] Maternal and infant prenatal variables include maternal height, parity, infant sex, gestational age and early neonatal length
[b] Maternal postpartum variables include morbidity, food security, diet diversity, weight velocity, and agricultural work; Infant postnatal variables include month starting the growth interval, morbidity, breastfeeding, vaccination and childcare
[c] All models control for village as a fixed effect
[d] Mean ± SE
[e] Model 1 consider maternal and infant prenatal variables, season starting growth interval and interactions; variables with p >0.1 were not included in final models
[f] Model 2 adds infant postnatal variables; variables with p >0.1 were not included in final models
[g] Model 3 adds maternal postpartum variables; variables with p >0.1 were not included in final models
[h] Model 4 adds interactions; variables with p >0.1 were not included in final models

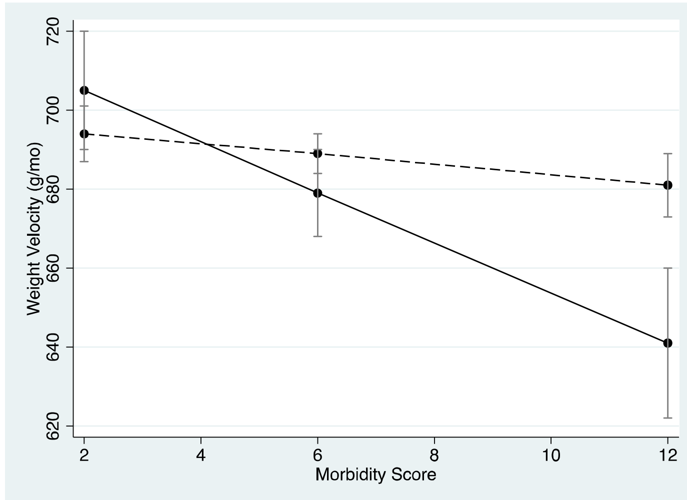


Figure 5.3 Relationship between morbidity score and rate of infant weight growth (g/mo) depending on infant vaccination status (interaction p=0.072) (dashed line represents vaccinated infants; solid line represents unvaccinated infants)

5.5 Discussion

The objective of the present study was to examine the association between season, and maternal and infant pre- and postnatal variables hypothesized to be related to length and weight velocity in the 1-4 month growth interval. This study provides new insights as to the important pre-and postnatal predictors of growth during the first six months of life in a novel study context. These insights are important for several reasons. First, they add to a limited knowledge base about rates of growth during early life. This information provides potentially new insights to help researchers and policy-makers understand why such high levels of undernutrition exist in early life in South Asia. Second, they highlight potentially modifiable factors (e.g. breastfeeding, vaccinations and care practices, etc.) that may serve as targets for public health interventions to treat and prevent undernutrition in young infants throughout the year. Lastly, the findings from this study will help inform location, study design, and measurement decisions for future seasonality studies.

Season

In Chapter 4, we observed a significant association between month of year (as defined by growth data) starting the growth interval and rate of length but not weight growth. One potential explanation is that weight is a more labile measure of infant growth and thus a three-month interval of growth may have been too long to observe an association, if one had existed. As a result of the small sample sizes in many of the months, we collapsed months of year into two seasons based on previously reported descriptive growth data (**Chapter 4**). Although this approach is likely an oversimplification of the variation in risk factors that occurs throughout the year, it allowed for sufficient sample size to test possible interactions. These interactions were important to consider because of the known interrelationship between many of the determinants of maternal and child undernutrition (e.g. infection and dietary intake) [24, 169]. In addition, because we did not find any evidence to support our hypotheses that maternal postpartum and infant postnatal determinants mediated the relationship between month of year and rate of postnatal growth (**Appendix D**), we were interested in exploring whether these determinants had differential associations with rate of growth depending on season. In simple univariate regression models of season and maternal and infant risk factors, we observed that the "higher-risk" season was associated with increased child morbidity (p=0.126) and maternal morbidity (p=0.002), higher odds of exclusive breastfeeding (p=0.118), increased childcare (p=0.064) and lower odds of receiving age appropriate vaccinations (p=0.047), relative to the "lower-risk" season. This suggests, albeit with weak evidence, that risk factors for poor infant growth and undernutrition are associated with season, as we defined it in this study.

In multivariable regression models, season significantly modified the relationship between childcare and rate of length growth. When growth began in the "lower- risk" season, no significant association was observed, but when growth began in the "higher-risk" season (August-October 2015), each minute increase in childcare was negatively associated with rate of length growth. The direction of this association may indicate possible reverse causality if mothers spend more time in childcare during the "higher-risk" season while caring for sick infants. In our sample, the "higher-risk" season was marginally significantly associated with increased mean infant morbidity score (p=0.126) and time spent in childcare (p=0.064), as compared to the "lower-risk" season, lending some support for this hypothesis. Contrary to findings from a few previous studies [99, 170], we did not find any evidence that season modified the relationship between rates of growth and either breastfeeding or infant morbidity.

<u>Maternal and infant time-independent fixed characteristics</u>

Among the fixed characteristics examined, the negative association between female sex and growth velocity is consistent with previous literature [162, 171, 172]. Maternal height was significantly positively associated with infant length growth, but not weight velocity, while the reverse was true for primiparity. Relatively little is known about the association between parity and early postnatal growth, and the available literature shows mixed findings. Some studies show no association between parity and either measures of early postnatal growth velocity or attained size at six months of age, while others have shown a negative association between parity and rates of early postnatal length growth, but not weight gain [162, 172, 173]. In contrast, a negative association between maternal stature and postnatal growth has been reported in a few previous studies [171, 172]. Although the underlying mechanism of this association is not fully elucidated, it is generally thought to reflect a transfer of intergenerational circumstances [171]. The degree to which chronic maternal undernutrition affects the quantity and quality of breastmilk is still open for debate, but some authors have theorized that the negative association between postnatal growth and maternal stature may be mediated by poor quantity and/or quality of breastmilk, a hypothesis we were unable to explore in the present analyses [49, 163, 171]. The more labile nature of the weight measures could possibly explain why we did not observe an association between maternal height and infant weight gain over the three-month interval of growth.

Newborn length and weight were significantly associated with rate of later infant length, and weight gain, respectively, but in opposite directions. Longer newborn infants (measured within seven days of birth) were observed to grow in length more slowly than shorter newborn infants, while heavier newborn infants were observed to grow more rapidly in weight than lighter newborn infants. In one study conducted in rural Guatemala, Delgado and colleagues observed a similar association between birth-length and length growth between birth and three months of infant age [172]. In contrast to our results, however, they showed that lighter babies at birth also experienced a greater rate of gains in weight from birth to three months [172]. In rural Peru, Iannotti and colleagues observed results that parallel those in the present study. The authors reported that birthweight was positively associated with rate of weight gain during the first postnatal month, while birth-length was negatively associated with rate of length gain [162].

The underlying mechanism for the different directions of association between newborn weight and length and rate of postnatal growth may be related to potentially non-concurrent timing of rate of weight and length growth, as suggested in a few other studies [85, 151]. Different postnatal growth patterns may also be related to differing patterns of morbidity as previously observed in chronically (born with low weight proportional to length) versus acutely (born light for length) growth restricted infants [1, 174, 175]. For example, if acute growth restriction was an important contributing factor to lower newborn weights in our sample of infants, these light-for-length (low

PI) infants may have continued to grow more slowly in weight during early postnatal life due to an increased risk for various morbidities [174, 175]. We were, however, not able to test these hypotheses in the present analyses. Lastly, we must consider that regression to the mean may have played a role in these findings, especially if the errors associated with length measurement were greater than the errors associated with weight measurement. We could have tested whether controlling for one-month infant growth measurements in regression analyses affected our estimations, however, we had the challenge of missing data for anthropometry measured at this age. We conducted extensive anthropometry training and standardization (**Chapter 2**) and achieved very low levels of measurement error associated with enumerator's measures of infant length. These procedures reduce the likelihood that regression to the mean was a significant contributing factor to observed results from regression models in the present study.

Infant time dependent postnatal risk factors

The associations between individual infant postnatal variables and rate of weight and length growth were generally consistent with the direction of associations reported from previous research, but of lesser magnitude and statistical significance [65, 176, 177]. Much of the previous research, however, has been conducted in infants that were older than infants in our sample. Limited research has been conducted on infant receipt of vaccinations and early postnatal growth rates. In one study in Guinea-Bissau, however, administration of the BCG vaccine to low birthweight (LBW) infants resulted in no effect on growth during the first year of life [178]. We observed that infant vaccination significantly modified the relationship between morbidity and both weight and length gain, such that a negative association was observed only for vaccinated infants. One possible explanation is that, in our sample, vaccination status served as a reflection of overall exposure to the health system, and thus an indication that infants received medical care when they were ill. The receipt of vaccinations may also have protected against illness severity, such that those vaccinated were overall less sick, and therefore less likely to have illness affect their growth. It is also possible that infants less than six months of age are afforded some protection from infection via breastfeeding and protection from environmental pathogens via maternal care, such that when vaccines were provided, no association is observed [16]. We did not, however, observe any significant associations between childcare, breastfeeding and infant morbidity score in our sample.

Lastly, our maternal morbidity score, which was constructed based on maternal recall, may have been too imprecise to adequately capture the relationship with rate of weight gain or length growth. This may also have been the case for our exclusive breastfeeding variable. The relatively small positive association observed between exclusive breastfeeding and growth velocity during this interval of growth may indicate that this variable, and the assumptions required to construct it, did not adequately capture the dynamics of breastfeeding practices that likely change with infant age [67]. At each monthly visit, our data on exclusive breastfeeding were based on a single 24-hour recall. Our variable could be biased if, for example, infants were inaccurately classified as exclusively breastfed because the mother had no access to other liquids or food items normally given to the infant since the last visit. We conducted sensitivity analyses in which we attempted to specify the exclusive breastfeeding variable during the interval as none, partial or exclusive. We observed that rates of weight and length growth were marginally significantly lower only in the partially breastfed group as compared to the exclusively breastfed group ($p=0.134$ and $p=0.071$ for models of weight and length velocity, respectively)

<u>Maternal time dependent postpartum risk factors</u>

In multivariable regression models, we observed evidence of a significant association between rates of growth and just two maternal variables (morbidity and work in agriculture). In our hypothesized causal chain, maternal variables were more distally related to infant growth rate, relative to infant risk factors. Therefore, variation in other available maternal variables (e.g. food insecurity, diet diversity and changes in maternal weight, etc.) may have been captured by the inclusion of variables located more proximally on the hypothesized causal chain. We did not, however, observe any evidence of this in exploratory univariate analyses among maternal variables. Another explanation for the lack of an association, had it existed, may be the imprecise nature of our maternal variables. Changes in maternal weight in the 1-4 month growth interval were based on the postpartum weights of the mother, and cannot be interpreted relative to either pre-pregnancy weight or gestational weight gain. Food insecurity and diet diversity were also measured less frequently than other postnatal measures and were likely weak markers of maternal diet.

In the present analyses, maternal morbidity was marginally associated with rate of infant length growth (p=0.081), but not weight gain, in an unexpected direction. It is possible that maternal morbidity scores, similar to child morbidity scores, are an imprecise measure of illness in the mother, or at least an inaccurate measure of the types of illness that may be expected to influence care and feeding practices. Another possible hypothesis is that mothers with higher morbidity scores spend less time away from home, and therefore spend additional time caring for the infant. In our sample, each minute increase in time spent in childcare (presumably at home) was associated with a marginally significant increase in maternal morbidity score (p=0.090), which provides some limited support for this hypothesis. We were unable to identify other comparable studies in the literature to determine if such findings have been observed in other developing country settings.

Our multivariable regression analyses also revealed the importance of maternal work in agriculture for rate of both infant weight and length gain, with some caveats. In models with rate of length growth as the dependent variable, we observed a significant negative association only between mothers who worked an intermediate amount of time in agriculture relative to those who worked the least amount of time in agriculture. In contrast, for models with rate of weight growth as the dependent variable, a significant negative association was observed only for mothers who worked the most amount of time in agriculture relative to those who worked the least amount of time. Time spent working in agriculture is likely related to more proximal infant risk factors, such as childcare and breastfeeding. We observed that those mothers who worked the most amount of time in agricultural work spent significantly less time in childcare ($p<0.001$), but did not have lower odds of exclusive breastfeeding. It is not entirely clear, however, why time spent in agricultural work is differently associated with changes in infant weight compared to length. One possibility is that the relatively more labile nature of infant weight measured over three month intervals added unwanted sources of variation to the analyses. This added variation may have made it more difficult to detect an association with agricultural work, especially in the intermediate work group where the sample size was relatively small.

To our knowledge, the association between work in agriculture and early postnatal growth has not been examined previously, and these relationships should be studied in future research with more specific measures of the types of agricultural work that women perform. In our sample, we observed that the mean time spent in agricultural work was very low. In addition, nearly 60% of mothers reported no participation in agricultural work at any visit between two and four months of infant age. These findings may indicate that women in Shivgarh refrain from work in agriculture during the early postpartum period, as observed in some other developing-country settings [40]. Another possibility is that our activity recall inadequately elicited the intended response from mothers and/or that a single 24-hour recall at each visit did not sufficiently represent the nature of agricultural work, which may have been sporadic.

This study has the advantage that it employed a longitudinal design with integrated measures of infant growth and important determinants of nutritional status. Few studies have measured growth velocity in the 0-6-month age group, and this study provides new insights as to the pre-and postnatal influences on early postnatal growth. A study of the association between potential risk factors and growth velocities, as opposed to attained size, allows for a better understanding of the process through which infants may become undernourished. This information may help to identify potentially modifiable factors that researchers and policy makers can target for future interventions to prevent undernutrition at an earlier stage, as compared to relying on attained size as an outcome.

This study also has several limitations. First, likely due to logistical field constraints, we had a challenge of missing data. We used a full information maximum likelihood statistical method to handle these missing data, under the assumption of MAR. Compared to other common statistical methods to handle missing data, such as multiple imputations, the full information maximum likelihood method is simpler to implement. Some studies have also shown that the full information maximum likelihood procedure produces relatively less biased estimates under conditions of MAR [179]. We conducted sensitivity analyses in which data were analyzed without the maximum likelihood procedure. Compared to models implementing the maximum likelihood procedure, we observed some differences in the statistical significance of the association between growth velocity and a few variables, mostly maternal fixed variables. We, however, observed no meaningful differences in overall model inference. Therefore, we assumed that the potential for bias would have been greater under the scenario in which the maximum likelihood procedure was not used.

We handled missing data in monthly infant postnatal and maternal postpartum data by taking the within child or mother mean of data from all available visits between two and four months of infant age. Although cross-sectional analyses suggested no age trend for any of the variables, except for exclusive breastfeeding, there is still potential for within-child variation that we could not adequately understand because of missing visits. This approach may have reduced the statistical significance of possible associations in the analyses, although the direction of this potential bias is unclear. Our approach to handling the exclusive breastfeeding variable, for which an age trend was observed, involved several assumptions that may or may not be true in a population where breastfeeding behaviors are likely to be fairly dynamic [67].

Lastly, it is possible that Shivgarh was not an ideal location to examine the possible associations between season and rates of infant growth. Most previous seasonality research has been conducted in settings where the agricultural cycle was not dependent on irrigation. Therefore, in previously published research, the impact of season on health and nutritional status was generally easier to detect, at least for older children [73, 96]. This study, in contrast, was conducted in a population in rural India that largely practices irrigated agriculture. We also studied the youngest infants who would be expected to have the most protection from breastfeeding. In irrigated agricultural systems, the meaning of "season" may differ from rain-fed systems. For example in Shivgarh, access to irrigation allows for multiple cropping cycles each year, which would be expected to reduce seasonal food shortages. Evidence that our sample was relatively food secure throughout the year provides some support for this assumption. Access to irrigation, a factor that likely ameliorates reduced food availability throughout the year, may partially explain why we did not observe stronger associations between season and rate of growth in our sample. Irrigation, however, would not be expected to reduce other risk factors that are likely to vary throughout the year, such as infectious disease pathogens and agricultural labor demands. A greater number of cropping cycles per year likely increase the demand for agricultural labor, with potential negative consequences for both mothers and infants (e.g. more separation between mothers and infants and possible negative effects on infant care and feeding practices, etc.). Another possibility is that, despite potential seasonal differences in risk factors for poor health and nutritional status, our sample had resources available to them that allowed for the implementation of successful coping strategies to prevent a worsening of the nutrition situation due to seasonal stress. We do not however, have data to test this hypothesis.

In conclusion, this is one of the few studies to report on the determinants of the rates of postnatal growth in weight and length in a nutritionally at- risk population in rural India where irrigated agricultural practices are pervasive. Prenatal factors continue to play an important role in determining growth between one and four months of infant age, but only partially explain the observed variation in early postnatal growth rates. Infant postnatal and maternal postpartum factors, such as exclusive breastfeeding, maternal morbidity and maternal work are also potentially important determinants of growth during the first six months of life. These determinants in the postnatal period represent potentially modifiable factors that could serve as targets for future intervention to treat and prevent undernutrition in early life. After controlling for other important determinants, season, as we have defined it based on growth data, as opposed to agro-climatic data, does not appear to be a strong predictor of postnatal growth in Shivgarh. We did, however, observe some limited evidence that the association between more proximal determinants of poor growth and undernutrition and postnatal growth rates may differ depending on season. This relationship may be stronger in settings with fewer resources, such as access to irrigation. These relationships should be better explored in other longitudinal datasets from diverse agricultural communities with frequent measures of growth and risk factors for poor growth during the first six months of life.

Chapter 6
Overall Discussion

6.1 Introduction

The primary objective of this research was to examine monthly variation in infant weight and length growth between birth and six months of age in a rural agrarian community in Uttar Pradesh, India. In this chapter, we summarize findings from the present research and discuss these findings in the context of previously published research. We then discuss the strengths and limitations of this study and lessons learned. Finally, we propose directions for future seasonality and growth research.

6.2 What have we learned? Comparisons to published literature

In this section we discuss overall seasonal patterns in young infant growth, followed by patterns of attained size and growth velocity in infants between birth and six months of age, and finally the predictors of growth during the first six months of life.

6.2.1 Season and growth

To our knowledge, this is one of the few studies to examine the association between month or season of the year and growth across both the pre- and postnatal periods in an irrigated agricultural setting. In Chapter 3, we observed that after controlling for potentially confounding factors (infant sex, gestational age, maternal height, parity, maternal education and food insecurity) mean early neonatal lengths and weights were significantly lower than the overall sample means for infants conceived between April and June 2014 and July and September 2015, respectively. These findings add new information to an existing body of literature that supports an association between month of birth and birth size. Compared to other previously published studies, however, the timing of the peak and nadir of mean early neonatal weights and lengths appears to occur during different periods of the year [39, 90, 93]. Adverse effects on fetal growth are likely to depend on the time during pregnancy when the insult occurs [94, 140]. It is therefore not surprising that the timing of insults to fetal growth may vary in settings with different underlying climatic and agricultural cycles.

In Chapter 4, we observed that within all examined three-month postnatal age intervals, there was a tendency for rate of length growth to be lower than the overall sample mean rate of length growth when the interval of growth began between August and October 2015. Compared to the other three-month growth intervals, however, the 1-4 month interval appeared to be more sensitive to the month of the year starting the interval. We found no association between rate of weight gain and month of year at the start of the growth interval. Prior to this research, the association between time of the year and rates of postnatal growth during the first six months of life had not been extensively studied, especially in irrigated agricultural regions in low-resource settings [96, 98]. The limited available literature, however, documents more substantial monthly and seasonal differences in rates of growth than we observed in the present study. Consistent with findings from other published research conducted in South Asia [154, 180], however, we observed high prevalences of stunting, wasting and underweight from birth. These prevalence estimates changed relatively little between birth and six months of age in our sample.

In Chapter 5, we observed that season was no longer a significant predictor of rate of length growth in the 1-4 month growth interval after controlling for maternal and infant fixed, or time-invariant, characteristics (infant sex, maternal height, parity, village). Various maternal postpartum and infant postnatal determinants (exclusive breastfeeding, maternal morbidity and maternal work in agriculture), however, emerged as important predictors of growth. We did not find any supporting evidence that maternal postpartum and infant postnatal risk factors, considered individually, acted as mediators of an association between season and rate of length growth in the 1-4 month growth interval. Therefore, we considered that season might have acted as a modifier of the relationship between maternal and infant factors and postnatal growth. We observed that the association between minutes spent in childcare and rates of length growth depended on season. We did not, however, observe any evidence that the association between rate of gains in weight or length and other proximal risk factors for undernutrition, such as exclusive breastfeeding and infant morbidity, depended on the season of growth. Some previously published research has reported either monthly or seasonal variation in these risk factors, but few researchers have examined the relationship between seasonality of these risk factors and infant growth [100, 108, 170]. The occurrence of monthly or seasonal differences in these risk factors for poor health and nutritional status may depend on the nature of agricultural work and cultural beliefs and practices that govern how mothers from agrarian communities manage work and childcare demands [101]. Studies specifically designed to examine these complex interactions should be a priority for future research.

6.2.2 Growth during the first six months of life

<u>Patterns of attained growth and growth velocities</u>

In Chapter 4, we conducted descriptive analyses of attained size by infant age and rates of weight and length growth in various three-month growth intervals during the first six months of life. We observed that infants were born small and then remained small through six months of age. Attained size and growth velocities were approximately -1 SD lower than the Multi Centre Growth Reference Study standard (MGRS). Mean weight-for-age Z-scores (WAZ), length-for-age Z-scores (LAZ) and weight-for-length Z-scores (WLZ), and the prevalences of underweight, stunting and wasting remained relatively stable between one and six months of infant age. We observed increased prevalences of these undernutrition indicators between birth and one month of age, but this increase may have been an artifact of a select group of infants captured at birth. The high proportion of growth faltering observed in our sample at birth, however, is consistent with findings from the few other published studies [9, 13, 180]. Available literature comparing growth in South Asian infants to the MGRS standard, shows that WAZ and LAZ are low at birth and, then steadily decline thereafter, but more dramatically after six months of age. Compared to a similarly conducted longitudinal growth study in Bangladesh) the patterns we observed in mean LAZ and WAZ from one to six months of age were generally consistent, but with slightly less decline with age. In contrast, however, mean WLZ in our sample declined much more steadily with age from birth [154]. The prevalence of wasting in our sample was high (around 17%), but slightly lower than results reported from nationally representative survey data in India [12]. An examination of patterns of growth from 6-9 and, 9-12 months of infant age in this dataset has not yet been conducted, but these analyses would help to determine whether these observed patterns persist, or whether these infants deviate further from the MGRS standard after six months of age.

<u>Potential linkages between weight and length growth</u>

In recent years, the possible linkages between the timing of weight and length growth has been revisited in the literature [85]. The results of earlier studies conducted in severely malnourished children suggested that after an insult to growth, infants needed to re-gain a certain percentage of lost weight before improvements in length gain were observed [151]. These findings may reflect the importance of adipose tissue in nutrient signaling for the control of growth hormone and other related growth processes [83, 85]. More recent literature suggests that variability in weight in early life may be linked to risk for linear growth faltering and stunting by one year of age

[85, 98]. We had only a single measure of newborn size to reflect fetal growth, and so our data can provide only limited insights regarding the dynamics of fetal and postnatal growth rates. We did, however, have growth data available for two non-overlapping infant age intervals (0-3 and 3-6 months). To explore whether there may be a possible linkage between weight and length growth in our sample, we examined the association between rates of weight growth in the 0-3 month growth interval with rates of length growth in the 3-6 month growth interval.

In simple univariate regression models, we found that a lower rate of weight gain in the 0-3-month growth interval was significantly associated with a lower rate of length gain from 3-6-months of age, and with increased odds of stunting at six months of age. After controlling for rate of length gain in the 0-3 month interval as a covariate in these two models, the significant associations remained. Based on these exploratory analyses, one can hypothesize a lagged effect of rate of weight gain on rate of length gain. We also observed, however, that rates of weight and length growth were positively associated within each three-month age interval (0-3, 1-4, 2-5 and 3-6 months). Therefore, there is some evidence, albeit limited, for some concurrent changes in rates of weight and length gain. Concurrent changes in rates of weight and length gain have also been previously reported in the literature [162].

A sizable body of research illustrates the associations between poor growth in early life and nutrition and health status during childhood and even later in life [3, 16, 28]. Additional research with the capacity to measure trimester-specific fetal growth velocity in combination with more frequent measures of postnatal growth is needed to answer some of these important underlying questions about growth processes and potential linkages between fetal and early and later infant postnatal growth.

6.2.3. Predictors of growth during the first six month of life

In Chapter 5, we found that both maternal and infant fixed, or time-invariant, characteristics (infant sex, maternal height, parity, village) and maternal postpartum and infant postnatal time-variable determinants (exclusive breastfeeding, maternal morbidity and maternal work in agriculture) were important predictors of growth between one and four months of infant age. We also observed that the association between childcare and length velocity depended on the season when growth began. The association between infant morbidity and both weight and length growth depended on the vaccination status of the child.

Postnatal time dependent infant risk factors

Many of the postnatal factors we identified as important predictors of growth velocity from 1-4 month of infant age, especially exclusive breastfeeding and infant morbidity have been, examined individually, or in some combination, in previous studies [64, 127, 177]. Most of the previously published research, however, does not include as many measures of risk factors for poor health and nutritional status as in the present research.

Previous research findings from low-resource populations suggest that exclusive breastfeeding is positively associated with infant growth. Research in Bangladesh [181], and a recent review of breastfeeding in 14 countries [68] have also shown that adherence to WHO recommendations for breastfeeding during infancy has a positive association with both length and weight gain, with a more consistent positive association observed for weight gain [2, 68, 181]. In contrast, we observed no relationship between exclusive breastfeeding and rate of weight gain but a consistent positive association between exclusive breastfeeding and rate of length gain in the present study. The lack of an association with weight gain may have resulted in part from our inability to capture the more labile nature of the weight measured within a three-month growth period. Other field-based epidemiological studies in developing countries reported mixed findings with regards to the magnitude of the negative effects of sub-optimal breastfeeding practices on infant growth [15, 65, 182].

The association between early child growth and various illnesses has also been examined in the literature, but often in older infants and children. In this study, we did not observe a strong association between rates of either weight or length growth and maternal recall of any individual infant illness symptoms, including diarrhea and respiratory infection symptoms. We did, however, observe an association between rates of weight and length growth and an overall morbidity score, but only in the group of infants who did not receive any age-appropriate vaccines. Diarrhea is one of the most common and nutritionally relevant illnesses in children from developing countries [183-185]. Studies of diarrhea in young children, often conducted in infants older than six months of age, have consistently shown a negative association between the frequency and/or duration of diarrhea on both gains in weight and length or height, with a less consistent association for the latter [56, 57, 186, 187]. The relationship between other morbidities, such as acute respiratory infections, and child growth is less clear, but some studies have shown negative effects on growth [188-190]. The association between morbidity and growth may be weak in in the current study due to protection afforded via breastfeeding and relatively less exposure of the young infant to the environment outside of the mother (e.g. not independently exploring the environment). This may explain why a global measure of illness captured the relationship between rates of growth and infant morbidity better than individual morbidity symptoms in our sample, and why an association was only observed for the group of unvaccinated infants. We did not, however, see any differences in morbidity score that depended on breastfeeding status of the child, an interaction reported in some developing countries contexts [170]. The reasons for the lack of an observed association are not entirely clear, but may be related to the relatively low proportion of women who did not breastfeed at all (assuming some breastfeeding also provides some benefit). It might also be due to the imprecise measurement of exclusive breastfeeding and infant morbidity, and/or possible recall bias associated with our breastfeeding and morbidity questionnaires.

Inadequate care and feeding behaviors are also documented important risk factors for undernutrition in early life [53, 191-195]. In the present study, we were only able to assess time spent in childcare, but not the quality of this care. We did observe a small negative association between time spent in childcare and rate of length growth, but only when growth occurred in the higher-risk season. Our inability to capture the quality of the mother-infant interactions in the present study may partially explain why we did not observe stronger associations. Greater research investments are needed to understand the nature of early infant care and maternal time constraints in agrarian populations, an area of research that remains poorly understood [196].

<u>Prenatal time invariant maternal and infant risk factors</u>

Findings from previously published research that prenatal risk factors continue to be important predictors of early postnatal growth [162, 172, 180] are consistent with findings from the present research. In multivariable regression analyses of our longitudinal data, we observed highly significant associations between rates of weight and length growth and various prenatal factors, including infant sex, maternal height, parity and newborn size (marker of fetal growth). It is well established that maternal health and nutritional status during pregnancy are important determinants of fetal growth and, that fetal growth (measured as size at birth) is a significant predictor of the postnatal growth of the child [25, 26]. In the present study, we did not have precise measures of maternal nutritional status during pregnancy (e.g. dietary intake, gestational weight gain) to examine many of these associations satisfactorily.

In multivariable regression analyses of our longitudinal data, we did, however, observe significant associations between newborn weight and length and rates of postnatal growth in weight and length. These associations operated in opposite directions. In the early postnatal period, heavier newborn infants grew faster than lighter ones, while longer infants grew more slowly than shorter ones. Insults to ponderal and linear growth are generally considered to reflect more acute and chronic insults to fetal growth, respectively [174]. It is possible that the factors that constrained fetal growth in length, most likely during the second trimester of pregnancy, were ameliorated in the early postnatal environment, while the factors that constrained fetal growth in weight, most likely during the third trimester, may have carried over after birth. These dynamics of growth, however, are poorly understood.

Lastly, regression to the mean may have played a role in the negative association observed for newborn recumbent length and early postnatal rates of length gain. We conducted extensive anthropometry training and standardization protocols throughout the research study, to minimize random measurement error. Although we reported very low technical errors of measurements (TEM) for measures of infant length, we cannot completely disregard the possibility that regression to the mean played a role in the results of regression models, especially if the measurement error for length was greater than the measurement error for weight. We extensively trained, but did not follow a standardization protocol for weight as discussed in Chapter 2. Because the inter- and intra-observer error in weight was so small and below detection limits of the weighing scales, we did not have available TEM data for weight. Therefore we were unable to examine differences in TEM between weight and length measures in this study.

Maternal time dependent postpartum risk factors

Maternal health and nutritional status during pregnancy often carries over to a woman's health and nutritional status in the postpartum period, and thus can influence subsequent infant growth. Poorly nourished breast-feeding mothers may experience reduced lactation capacity, which could negatively affect infant growth. The degree to which lactation capacity is compromised in undernourished women and, if the high-energy costs of breastfeeding may exacerbate maternal depletion is still up for debate [16, 27, 28, 197].

In the present study, we had available postpartum measures for maternal morbidity, food insecurity, diet diversity and time spent in agricultural activities. We observed a negative association between rate of infant weight and length growth and maternal time spent in agricultural activities. The low participation in agricultural labor however, limits our ability to draw any strong conclusions from this finding. To our knowledge no other studies have examined the relationship between work in agriculture and early postnatal growth.

Among other time-dependent maternal characteristics measured in the postnatal period, we observed only a weak association between maternal morbidity and rate of infant growth in length. This relationship, however, is poorly understood in the literature, and some of our study limitations might suggest that this finding was specious. To our knowledge, no other studies have examined the relationship between maternal illness symptoms, such as those measured in the present study, and postnatal growth of the infant. Future research should seek to validate the use of maternal morbidity questionnaires with biochemical assessment and/or physician confirmation of illness. We did not observe any other significant associations of maternal variables with either rate of weight or length gain.

Measures of dietary diversity and food insecurity were measured less frequently during the postnatal period. Due to missing data, we frequently had only a single measure of food insecurity available for the1-4 month postpartum age period. A single measure is probably insufficient to assess associations with growth over the entire interval. Furthermore, diet diversity, recalled over a single 24-hour period, does not necessarily reflect diet quality for individual women, and may thus be an inadequate proxy for maternal diet [167]. Lastly our sample of women appeared to reflect a relatively food secure population. There may have been insufficient variation to observe an association between food insecurity and infant growth.

6.3 Strengths and Limitations of the present research

We addressed the strengths and limitations of this work as relevant in Chapters 3-6 and provide a brief summary here. Limited longitudinal data are available to understand growth during the early infancy period. The available analyses of infant growth data frequently comes from cross-sectional surveys that provide only limited insights into the dynamics of early growth faltering in high-risk subpopulations. The present study was therefore conceptually innovative because of the longitudinal design and the early period of life studied (birth to six months of age) in a developing country context. Few longitudinal growth studies have examined young infants in developing countries with a focus on agricultural and seasonal factors as we did in this study. We also collected a wide range of maternal and infant measures, and this approach allowed for an integrated examination of the potential predictors of growth rates rather than achieved growth during early life. In addition, few field based growth studies follow the strict anthropometry training and standardization protocol that we used in the present study. We demonstrated that successful training and standardization on anthropometry could be carried out in relatively remote village settings. Mothers tolerated repeated measurements taken on very young infants when the proper community relationships were established. Our enumerators achieved very low anthropometry TEM and bias throughout the study period, similar to those achieved in the MGRS study [120]. This extensive anthropometry training and standardization allowed us to minimize the random and systematic error in our measures of growth. Lastly, the majority of previous research on seasonality was conducted in rain-fed agricultural areas. The setting for this research was therefore novel because agriculturalists in Shivgarh predominantly practice irrigated agricultural practices.

There were several significant limitations of the present study that may have resulted in sample bias due to loss to follow-up, missing data, and the specific study context. The source of loss to follow-up bias was probably related to challenges involved in conducting research under field constraints, preventing us from achieving the targeted universal sample of pregnant women from our nine selected villages in Shivgarh during all recruitment months. Some of these field challenges included, but were not limited to, a small staff that was often unable to re-visit mothers who were temporarily not available for the selected visit, and who worked under difficult environmental conditions (extreme temperatures and rainfall). These factors may have increased the risk for selection bias in both the recruited sample and the sample of captured births, especially if, for example, staff were unable to reach more remote, and potentially poorer parts of our study area during some seasons of the year (e.g. monsoon season). We did not find any strong evidence of this in our analyses, but our sample sizes during some months of the year were smaller than anticipated. The reason for this was likely due to to the high workloads for our enumerators during these periods of the year. It is, however, also a possibility that an underlying seasonal pattern in birth frequencies throughout the year played a role in the differences in sample size in our birth cohorts [146]. We were unable to test this hypothesis in the present study, but we cannot fully exclude the possibility for selection bias in our recruited sample and sample of births.

A second potential source of bias related to the selection of our longitudinal sample, which had substantial missing data, was largely due to missed monthly visits. These visits were most frequently missed because the mother was temporarily unavailable and we were often not able to re-visit mother-infant pairs enough times within 14 days of the infant's monthly birthday to find the mother at home. We provided evidence to support our assumption of missing at random (MAR), and we handled missing data using a full information maximum likelihood procedure to reduce the bias associated with missing data on covariates. We maximized our sample size by utilizing a random slopes and intercepts model to estimate growth velocity in three-month increments based on all available data measured during interval. The use of three-month increments may, however, have contributed to our inability to detect an association between month of year and weight velocity, if one existed, because of the labile nature of infant weight. We were also not able to take full advantage of our longitudinal data in measurement of potential predictors of infant growth as a result of missing data. Moreover, we likely did not fully capture the dynamic nature of some of our measures, such as breastfeeding, across infant age as a result of these missed visits.

Last, the present research was conducted in an area where irrigated agricultural practices were ubiquitous. Although this feature added to the novelty of the study context, as discussed in Chapter 5, the nature of the agricultural system in Shivgarh may have ameliorated some aspects of seasonal stress (e.g. reduced food availability throughout the year). This may explain, in part, why we did not observe stronger associations between season and growth. In addition, we only observed women recruited during a single agricultural cycle. Based on time spent in the study area, we did not have reason to believe that this particular agricultural cycle was atypical of other years. We did not, however, observe the same patterns in growth in the months of overlap between 2014 and 2015 (August-October). This does not necessarily imply that there were differences in the agricultural cycle between these two years, but we cannot exclude this possibility. Examination of historic temperature, rainfall and agricultural data could potentially help to answer this question. Another location in rural India with more marked seasonal extremes may be more appropriate for future research about the mechanisms of seasonal stress.

6.4 Contributions to the field of nutrition and public health

6.4.1 A combination of standard methods in a unique setting

This study combined measures of anthropometry, and a host of infant (feeding, morbidity, care, vaccination, season starting the growth interval) and maternal measures (food security, diet diversity, morbidity, work in agriculture) measures that are generally not integrated in field-based nutrition studies, particularly for infants less than six months of age. Despite the above noted limitations, this combination of measures yielded some interesting findings with regards to the inter-relationship between several risk factors for poor health and nutritional status including morbidity and infant vaccination status, season and childcare, and maternal work in agriculture and early infant growth. These findings may provide important insights for hypothesis generation for future research.

In this study, we also recruited women continuously over 15 months, which allowed us to examine risk factors for poor health and nutritional status over the entire year during late pregnancy and the early postnatal period. Exposure to seasonal stress is a regularly occurring phenomenon in many developing countries, and few studies provide the opportunity to examine the potential impact of this exposure on growth during a high-risk period of early life. The high prevalences of undernutrition, especially wasting, during the first six months of life reported in this study are of public health significance and reiterate the need for greater research and program investments for this age group. Our findings that both pre- and postnatal risk factors were important determinants of early postnatal growth underscores the need for a life-cycle approach to combat high levels of undernutrition in early life in India.

To our knowledge, no other studies have examined seasonal variation and nutrition-agriculture linkages in a population with widespread access to irrigation. This new knowledge is significant because access to irrigation likely changes some important characteristics of the underlying agricultural cycle, which may ameliorate some monthly differences in risk factors for poor nutrition (e.g. food availability, income, etc.), and simultaneously increase monthly differences in other risk factors (e.g. labor demands, time constraints for childcare, etc.). These dynamics are, however, poorly understood. Future research should prioritize a more holistic understanding of seasonality in diverse agricultural systems (e.g. irrigated vs. rain fed, cash crop vs. subsistence crops, use of pesticides, etc.). Populations working within diverse systems are potentially exposed to a unique distribution of risk factors throughout the year, and may utilize distinct coping strategies for the amelioration of seasonal stress. This information would inform a much broader understanding of seasonality in the developing world.

6.4.2 Lessons learned for future research

Conducting longitudinal growth studies in rural settings of developing countries poses many logistical and methodological challenges. Such studies, however, have the potential to uncover important underlying causal factors for poor growth and nutritional status, and should be considered for future research. The results from this study came from nine selected villages in one district in Uttar Pradesh. This area is predominantly irrigated, which distinguishes it from many other parts of rural India and elsewhere in the developing world. Results from this study may not be applicable elsewhere, even within other agrarian populations in Uttar Pradesh. We observed evidence of a significant association between season and length velocity, but the magnitude of this association was small (0.064 cm/month) and not likely of public health significance. In retrospect, the effect size that we used to estimate the sample size for the present research was probably an overestimate. This is based on information from the present study that suggests that, as compared to rain-fed agricultural areas, the magnitude of seasonal variation in at least some of the risk factors for poor health and nutritional status is less in irrigated agricultural areas. As compared to populations residing in rain-fed agricultural areas, this population is likely less vulnerable to seasonal stress, as previously described. The reason why we were able to detect a statistically significant difference is likely due to the fact that the variability in the length measures in our sample were smaller than the variability in the measures from the MGRS standard, which was the basis for our sample size estimation. Our initial hypothesis that the association between month of year and rates of postnatal growth would be mediated by more proximal maternal and infant risk factors was not supported. In this study, however, we considered potential mediation only by individual risk factors and by disaggregated months of year. A better analytical approach should be to test for mediation by groups of risk factors, which may more precisely reflect the impact of a compilation of nutrition and health risk factors that co-vary by months or season of the year. We may also consider testing mediation by months of year collapsed into seasons to increase our sample size for these analyses. Longitudinal studies conducted in settings with greater seasonal extremes may also be better suited for the examination of seasonal mechanisms.

6.5 Directions for future research

This research contributes to a better understanding of growth patterns and the predictors of growth, as an indicator of undernutrition, between birth and six months of age in a novel study context [9, 13, 16]. Several research directions can be proposed to enhance the findings of this research. First, of high priority is the routine inclusion of infants between birth and six months of age in surveillance and longitudinal studies of infant growth. This will increase the availability of high quality data for this understudied age group and help researchers to disentangle the relative importance of pre-and postnatal risk factors for later postnatal growth. Carefully designed studies that allow for the assessment of the dynamics between rates of weight and length growth during the first six month of life and linear growth faltering in later childhood are also a high priority for future research investments. Longitudinal data collected at more frequent intervals during the first two years of life will allow for better analytical assessment of the hypothesized relationship between early growth faltering and attained size (e.g. stunting) by 1-2 years of age. Data available for infants at nine and 12 month of age from the present study may add additional insights about these relationships and should be analyzed as soon as possible.

In the present study, we observed prevalences of stunting, wasting and underweight that were very high at birth, and then relatively static between one and six months of infant age. We also found that both pre-and postnatal risk factors are important predictors of rates of postnatal growth during early infancy. These findings underscore the need for researchers and policy makers to increasingly adopt a life-cycle approach for understanding growth during infancy and childhood. More studies should be designed specifically to understand the timing of fetal growth, and how patterns of fetal growth influence growth in the early postnatal period. This includes, for example, studies to distinguish if or how common causal factors for poor growth carry over from the pre- to the postnatal periods. A carry over of risk factors may represent a continuity of circumstances from pre-to postnatal life [197, 198]. It may also, however, be more complex and represent epigenetic programming that occurred during fetal life [199, 200]. A better understanding of the underlying causal mechanisms for poor growth in early life may provide insights as to the best timing for interventions to prevent long-term adverse effects for later child growth and development as well as other poor health outcomes.

Nutritional status during the first six months of life is determined by a complex array of risk factors which must be considered from a more holistic and integrative perspective [16]. Future longitudinal studies of low-resource populations should include a greater number of measures of risk factors for poor health and nutritional status. These might include some of the measures included in the present research, such as time spent in agricultural work and childcare, or possibly other child outcomes, such as cognitive development. The integration of measures such as these into cross-sectional and longitudinal studies will allow for a better understanding of the potential range of consequences associated with nutrition insults during early life. Researchers should also strive to implement more innovative measurement methodologies in the field to collect more precise measures that are less dependent on maternal recall. One example would be the use of activity monitoring devices, such as accelerometers and GPS trackers, to better capture the energy expenditure and movements of rural women working in agriculture. Data collection methods could also include both quantitative and qualitative research methods to understand the nature of complex trade-offs that likely occur in rural agrarian settings, such as those between work and childcare. A real challenge exists in developing measurement tools to uncover potential common underlying linkages in agriculture-nutrition pathways that are applicable across populations and also modifiable to represent the context specific experience of work and care domains.

Lastly, the present study suggests that, compared to other settings, especially those where rain-fed agricultural practices remain, our sample from Shivgarh may not be as vulnerable to monthly or seasonal stress. Therefore, the findings from the current study should not mean that future research should disregard the potentially important influence of monthly or seasonal variation in risk factors on fetal and postnatal growth. The specific factors that determine individual vulnerability to seasonal stress under diverse agro-climatic conditions, and whether these factors vary by age and by year (e.g. different exposure to environmental pathogens, different yearly crop yields, food prices, occurrence of disasters, etc.) are not well understood. In future years, factors such as climate change, for example, are expected to result in more variable and less predictable agro-climatic patterns in much of the developing world [201]. Surveillance efforts to monitor potentially changing levels of monthly or seasonal risk for vulnerable mother and infant populations should be considered, even in areas such as Shivgarh, where seasonal extremes appear to be less severe than observed in other parts of the developing world.

Appendix A
Chapter 2

This appendix supplements the main text of Chapter 2. On four separate visits between May and August 2013, formative research was conducted in four villages of the Shivgarh block of Uttar Pradesh. These villages were purposefully selected by CEL field staff knowledgeable of the local area to be representative of typical villages in Shivgarh. The primary aim of the formative research was to understand patterns, especially seasonal patterns, in potential risk factors for poor health and nutritional status in this area. This formative work also informed the development of survey questionnaires.

We conducted eight semi-structured individual interviews and three focus group discussions (10-15 participants in each group) with pregnant and lactating women, local government health workers (ASHA and Anganwadi workers) and male agricultural workers. One focus group discussion included only pregnant and lactating women, while the other two focus groups were made up of a mixed group of participants. The interviews/focus group discussions were conducted primarily in Hindi by Community Empowerment Lab research staff (prepped in advance by E. Madan) and E. Madan observed. If additional follow-up questions were posed in English, CEL research staff translated from English to Hindi. The interviews/focus groups were organized around nine primary domains (seasons/seasonal patterns, infant feeding and care, infant health, maternal health, local practices during pregnancy and after childbirth, food security and diet diversity, social support systems, sanitation, and work in agriculture). Individual interviews lasted for approximately one hour, and focus group discussion lasted between one and two hours. We did not decide the amount of interviews/focus groups in advance, but rather continued our formative research until we reached the point that additional interviews/focus groups no longer yielded new information related to our primary domains.

Table A.1 provides additional detail to describe the source of questionnaire modules used in the current study. **Table A.1** illustrates the timing of administration of the various questionnaire modules throughout the study period. Tables **A.3-A.13** are copies of the English versions of the questionnaire modules administered to mothers in the present study.[10]

<u>Appendix A figures and tables</u>

Table A.1 Source of survey material and justification for use in the present research in Shivgarh, Uttar Pradesh

Module	Source	Measurement period	Justification for use
Household modules			
Household roster	IFPRI survey module	Current	Successfully used in previous IFPRI research in South Asia [202, 203]
Background information	IFPRI survey module	Current	Successfully used in previous IFPRI research in South Asia [202, 203]

[10] Only modules within the scope of the analyses within this dissertation are included in this appendix

Table A.1 (continued)

Assets Index	CEL developed index	Current	Data already collected by CEL under AMANHI project
Land/Livestock Ownership	IFPRI survey module	Current	Successfully used in previous IFPRI research in Nepal [202, 203]
Field Crops/Homestead production	Based on modified IFPRI survey (Suaahara) module and World Bank Living Standards Measurement study	Current cropping season/past cropping season	Best available tools found in review of previously conducted surveys in South Asia region [204, 205]
Public Distribution/Public works programs	IFPRI survey module	Past 30 days	Successfully used in previous IFPRI research in South Asia [202, 203]

Table A.1 (continued)

Maternal modules			
Pregnancy History	CEL developed survey module	Complete history	Data already collected by CEL under AMANHI project
Chronic illness	Module developed by medical doctor on CEL staff	Complete history	Developed based on best available local/medical knowledge
Tobacco and Alcohol Exposure	IFPRI survey module	Past 30 days/7 days	Successfully used in previous IFPRI research in South Asia [202, 203]
Health Contacts and Services Received	IFPRI survey module	Past 30 days	Successfully used in previous IFPRI research in South Asia [202, 203]
Maternal Depression	WHO SRQ-20 [206]	Past 30 days	Validated for use in low and middle income countries [207]
Household Food Insecurity	FAO Household Food Insecurity Access Scale [137]	Past 30 days	Developed for use in low and middle income countries; Used successfully in other parts of South Asia [208, 209] [202, 203]
24-hour diet recall	FANTA Minimum Dietary Diversity tool [167]	24 hours	Validated as indicator of diet quality[210, 211]
Morbidity recall	Johns Hopkins survey module	Past 30 days/7 days	Used successfully in previous research conducted in Uttar Pradesh (personal communication)
Hand-washing	Module developed by medical doctor on CEL staff	Past 30 days	Developed based on best available local/medical knowledge
Time allocation	Women's Empowerment index time allocation module [212]	24 hours	Used successfully in Nutrition-Agriculture Survey in Nepal (Suaahara) [202, 205]

Table A.1 (continued)

Infant modules			
Vaccinations	Developed by CEL research staff	Past 30 days	Based on Indian government recommendations for vaccination
Early initiation of Breastfeeding	WHO indicators for assessing infant and young child feeding practices	Variable depending on time of birth visit	Standard operations based on WHO guidelines [165, 213]
Receipt of supplements	WHO indicators for assessing infant and young child feeding practices	24 hours	Standard operations based on WHO guidelines [165, 213]
Morbidity recall	Johns Hopkins survey module	Past 30 days/7 days	Successfully used in previous research conducted in Uttar Pradesh (personal communication)
24-hour diet recall	WHO indicators for assessing infant and young child feeding practices	24 hours	Standard operations based on WHO guidelines [165, 213]

Table A.2 Summary of the different survey modules and timing of administration to mothers in Shivgarh[11]

Modules	Visits (10 total)									
	P	B	1	2	3	4	5	6	9	12
Household										
Household roster	X									
Background information	X									
Assets Index	X									
Land/livestock ownership	X									
Field crops/homestead production	X		X		X		X		X	X
Public distribution system/Public works programs	X			X		X		X	X	X
Maternal										
Pregnancy history	X									
Chronic illness	X									
Tobacco and alcohol exposure	X									
Health contacts and services received	X							X	X	X
Maternal depression (WHO SRQ-20)	X			X						
Household food insecurity	X			X		X		X	X	X
24-hour diet recall			X		X		X		X	X
Morbidity recall			X	X	X	X	X	X	X	X
Hand-washing			X							
Time allocation			X	X	X	X	X	X	X	X
Infant Modules										
Vaccinations		X	X	X	X	X	X	X		
Early initiation of breastfeeding		X	X							
Receipt of supplements			X	X	X	X	X	X		
Morbidity recall			X	X	X	X	X	X	X	X
24-hour diet recall				X	X	X	X	X	X	X
Anthropometry	X	X	X	X	X	X	X	X	X	X

[11] The 9 and 12 month visits were outside the scope of this dissertation

Name	Relationship to the head of the household	Other relationship	Sex	Age (Completed years or years and months for Children <5)	Marital Status	Other Marital Status	Education	Primary Occupation	Other Occupation

Figure A.3 Household roster module

Figure A.4 Assets index module (available from CEL)

Figure A.5 Pregnancy history module (Available from CEL)

Question	Outcome
In the past 30 days did you worry that your household would not have enough food?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days were you or any household members not able to eat the kinds of foods you preferred because of a lack of resources?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days did you or any household member eat just a few kinds of food day after day because of a lack of resources?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days did you or any household member eat food that you did not want to eat instead of other foods because of a lack of resources?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days did you or any household member eat a smaller meal than you felt you needed because there was not enough food	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days did you or any household member eat fewer meals in a day because there was not enough food?	1=yes, 2=no

Figure A.6 (continued)

How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days was there ever no food at all in your household because there were no resources?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days did you or any household member go to sleep at night hungry because there was not enough food?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)
In the past 30 days did you or any household member go a whole day without eating anything because there was not enough food?	1=yes, 2=no
How often did this happen?	1=Rarely (1-2 times) 2=Sometimes (3-10 times) 3=Often (>10 times)

Figure A.6 Household food insecurity module

Question	Outcome
Was yesterday a special day, like a celebration or feast day or a fast day where you ate special foods or more or less than usual or did not eat because of fasting?	1=Yes , 2=No (Ask question about day before yesterday)
Was the day before yesterday a special day, like a celebration or feast day or a fast day where you ate special foods or more or less than usual or did not eat because of fasting?	1=Yes, 2=No (Ask questions about day before yesterday)
CEREALS (e.g. Rice, roti, bread, puffed rice, pressed rice, noodles, or any other foods rice, wheat, maize/corn, or other locally available grains)	1=yes, 2=no
VITAMIN A RICH VEGETABLES AND TUBERS (e.g. Pumpkin, carrots, sweet potatoes that are orange and yellow inside)	1=yes, 2=no
WHITE TUBERS AND ROOTS OR OTHER STARCHY FOODS (e.g. Potatoes, white yams, white sweet potato (not orange inside) or other foods made from roots)	1=yes, 2=no
DARK GREEN LEAFY VEGETABLES (e.g. Spinach, amaranth leaves, mustard leaves, pumpkin leaves, yam leaves, etc.)	1=yes, 2=no
OTHER VEGETABLES (e.g. Cauliflower, cabbage, eggplant, green papaya, radish, onion, etc.)	1=yes, 2=no
VITAMIN A RICH FRUITS (e.g. Ripe mangoes, ripe papaya, apricot, jack fruit etc.)	1=yes, 2=no
OTHER FRUITS (e.g. Tomatoes, Bananas, apples, guavas, oranges, other citrus fruits, pineapple, watermelon, grapes, strawberries, plum, peaches etc.)	1=yes, 2=no
Meat (e.g. Goat, lamb, buffalo, pork, chicken, duck, or other birds, liver, kidney, heart, lungs etc.)	1=yes, 2=no
EGGS (e.g. Eggs of different birds – chicken, duck, etc.)	1=yes, 2=no
FISH (e.g. Big/small fresh or dried fish or shellfish such as prawn, crab etc.)	1=yes, 2=no
BEANS, PEAS OR LENTILS (e.g. Soybeans, beans, peas, lentils, other pulses)	1=yes, 2=no
MILK AND MILK PRODUCTS (e.g. Milk, cheese, yogurt, or other milk products)	1=yes, 2=no
NUTS AND SEEDS	1=yes, 2=no
OILS AND FATS (e.g. Oil, fats, or butter added to food or used for cooking including ghee)	1=yes, 2=no
SWEETS/SNACK FOODS (e.g. Sugar, honey, rock candy, chocolates, biscuits, cold drinks, chips)	1=yes, 2=no
TEA/COFFEE	1=yes, 2=no
Any other food?	1=yes, 2=no

Figure A.7 Maternal dietary recall module

Question	Outcome
Have you had productive cough/rapid breathing or grunting/wheezing in the past 30days(since our last visit)?	1=yes, 2=no, 88=don't know
How many of the past 7 days did you have productive cough/rapid breathing or grunting/wheezing?	
How many of these days did you have to stop doing your usual activities?	
Have you had blood in the sputum in the past 30days(since our last visit)?	1=yes, 2=no, 88=don't know
How many of the past 7 days did you have a blood in the sputum?	
How many of these days did you have to stop doing your usual activities	
Have you had fever with or without chills in the past 30 d?	1=yes, 2=no, 88=don't know
How many of the past 7 days did you have fever with or without chills?	
How many of these days did you have to stop doing your usual activities	
Have you had a Nausea/vomiting in the past 30days(since our last visit)?	1=yes, 2=no, 88=don't know
How many of the past 7 days did you have a nausea/vomiting?	
How many of these days did you have to stop doing your usual activities?	
Have you had loose watery stools ($\geq$ 4 times/day) in the past 30days(since our last visit)	1=yes, 2=no, 88=don't know
How many of the past 7 days did you have loose watery stools ($\geq$ 4 times/day)?	
How many of these days did you have to stop doing your usual activities?	
Have you had a severe headache in the past 30days(since our last visit)?	1=yes, 2=no, 88=don't know
How many of the past 7 days did you have a severe headache?	
How many of these days did you have to stop doing your usual activities?	
Have you had any injury in the past 30days(since our last visit)?	1=yes, 2=no, 88=don't know
What was this injury?	1=severe cut on body part, 2=sprained/broken bone, 3= eye injury, 97=other
How many of the past 7 days did you have this injury?	
How many of these days did you have to stop doing your usual activities?	

Figure A.8 Maternal morbidity recall module

Activities	Morning (4am -4pm) (720 minutes)	Afternoon (4pm- 4am) (720 minutes)
In the past 24 hours, how much time did you allocate to: Sleeping and resting		
Personal care (eating/drinking/hygiene)		
School (also homework)/Work (for self or as employed for others)		
Farming/livestock/fishing		
Domestic work (shopping/getting service, cooking, weaving, sewing)		
Care for children		
Care for adults/elderly		
Leisure/ Social and religious activities (e.g., watching T.V./ listening to radio/reading/ roaming around/playing/talking on phone)		
Other (Specify) ____________		
Total Time		

Figure A.9 Time allocation module

Question	Outcome
BCG (injection in the arm or shoulder that usually causes a scar)?	1=yes, 2=no, 88=don't know
OPV 0 (drops in the mouth)	1=yes, 2=no, 88=don't know
Hep-B-0 (An injection usually given in the thigh)	1=yes, 2=no, 88=don't know

Figure A.10 Infant vaccinations module

Question	Outcome
In the last month, since our last visit, did you introduce any new liquids (besides breast milk) to the infant for the first time?	1=yes, 2=no, 88=don't know
Which liquid/liquids did you introduce (multiple response)?	1=animal milk; 2=infant formula/powdered milk, 3=water; 4= honey; 5=sugar water; 6=tea; 7=dal water; 97=other
In the last month, since our last visit, did you introduce any new semi-solid or solid foods to the infant for the first time (e.g. biscuits, khicidi, porridge)?	1=yes, 2=no, 88=don't know
Which semi-solids/solids have you introduced? (multiple response)	1=biscuits; 2=porridge; 3=khicidi; 4= roti; 5= vegetables; 6=fruits; 7=yogurt; 97=other
Was yesterday a special day, like a celebration, feast day, fasting, sickness etc. in which (Name) ate special foods or more or less than usual or did not eat because of fasting?	1=yes, 2=no, 88=don't know
Was the day before yesterday a special day, like a celebration, feast day, fasting, sickness etc. in which (Name) ate special foods or more or less than usual or did not eat because of fasting?	1=Yes (Ask yesterday's diet) 2=No (Ask day before yesterday's diet)
Yesterday/day before yesterday during the day or night did (name) drink/eat any Plain water	1=yes, 2=no, 88=don't know
Was the infant given plain water in the past 7 d?	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any juice (Fruit juice)/juice drink	1=yes, 2=no, 88=don't know
Was the infant given juice in the past 7 d?	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Dal water	1=yes, 2=no, 88=don't know

Figure A.11 (continued)

Was the infant given dal water in the past 7 d?	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Animal milk	1=yes, 2=no, 88=don't know
Which type of animal milk?	1=COW, 2=BUFFALO, 3=GOAT, 97=OTHER, 88=DON'T KNOW
How many times?	
Was the infant given animal milk in the past 7 d?	1=yes, 2=no, 88=don't know
Which type of animal milk?	1=COW, 2=BUFFALO, 3=GOAT, 97=OTHER, 88=DON'T KNOW
How many times?	
Yesterday/day before yesterday during the day or night did (name) drink/eat any Powdered milk (Commercial baby food/formula, such as Lactogen, tinned, powdered milk etc.)	1=yes, 2=no, 88=don't know
How many times?	
Was the infant fed powdered milk (Commercial baby food/formula, such as Lactogen, tinned, powdered milk etc.) in the past 7 d?	1=yes, 2=no, 88=don't know
How many times	
Yesterday/day before yesterday during the day or night did (name) drink/eat any Tea, coffee or sugar water	1=yes, 2=no, 88=don't know
Was the infant given Tea, coffee or sugar water in the past 7 d?	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any other liquids?	1=yes, 2=no, 88=don't know
Which other liquid/liquids	
Was the infant given any other liquids in the past 7 d?	1=yes, 2=no, 88=don't know
Which other liquids?	
Was (Name) fed anything from a bottle or nipple yesterday during the day or night	1=yes, 2=no, 88=don't know
What was fed from a bottle or nipple?	1=animal milk, 2=powdered milk, 3=juice, 4=water, 5=tea, 97=other 88=don't know

Figure A.11 (continued)

Was (Name) fed anything from a bottle or nipple during the past 7 d?	1=yes, 2=no, 88=don't know
What was fed from a bottle or nipple?	1=animal milk, 2=powdered milk, 3=juice, 4=water, 5=tea, 97=other 88=Don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Biscuits	1=yes, 2=no, 88=don't know
Was (Name) given biscuits in the past 7 d?	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Milk products (e.g. yogurt, buttermilk, cheese and other milk items (paneer, khuwa etc.)	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any semi-solid or solid foods (e.g. porridge, mashed fruits or vegetables etc., roti, snack foods)	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Cereals Porridge, Rice, roti, bread, bun, etc. and any other food made from grain, millet, wheat, maize, barley, etc.	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any VITAMIN A RICH VEGETABLES AND TUBERS Pumpkin, carrots, sweet potatoes that are yellow or orange on the inside	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any WHITE TUBERS AND ROOTS OR OTHER STARCHY FOODS White potatoes, white yams, colocasia any other foods made from roots	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Dark green, leafy vegetables spinach, amaranth leaves, mustard leaves, clocasia leaves	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Vitamin A Rich fruits Ripe papaya, mangoes, or apricot	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Other fruits or vegetables banana, apple, guava, orange, tomato	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Meat (e.g. Chicken, duck, pigeon or other poultry pork, buffalo, lamb, goat, liver, heart, kidneys, lungs or other organ meats)	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Eggs	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Fish, Fresh or dried fish or shellfish	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Beans, peas, or lentils	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Nuts and seeds, peanuts, cashews, walnuts	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Fat and oils, oil, butter, ghee	1=yes, 2=no, 88=don't know

Figure A.11 (continued)

Yesterday/day before yesterday during the day or night did (name) drink/eat Maggi	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Panjeeri	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat any Sweets and Snack foods, Chips or chanachur, candies, chocolates, or other sweets	1=yes, 2=no, 88=don't know
Yesterday/day before yesterday during the day or night did (name) drink/eat Other Semi-solid/solid Food?	1=yes, 2=no, 88=don't know

Figure A.11 Infant feeding/24-hour recall module

Question	Outcomes
Has (child's name) had productive cough, rapid/fast breathing, Grunting or wheezing, or chest in-drawing in the past 30 d?	1=yes, 2=no, 88=don't know
How many of the past 7 days did the child have productive cough, rapid/fast breathing, grunting or wheezing, or chest in drawing?	
Has (child's name) had fever in the past 30 d?	1=yes, 2=no, 88=don't know
How many of the past 7 days did the child have fever?	
When (NAME) had a fever, how much liquid did (NAME) receive during the time he/she had a fever. READ RESPONSE CATEGORIES	1=Less 2=ABOUT THE SAME 3=MORE 4=NOTHING TO DRINK 88=don't know
Has (child's name) had Vomiting in the past 30 d?	1=yes, 2=no, 88=don't know
How many of the past 7 days did the child have vomiting?	
Has (child's name) had loose watery stools, $\geq$ 4 times/day in the past 30 d?	1=yes, 2=no, 88=don't know
How many of the past 7 days did the child have loose watery stools , $\geq$ 4 times/day?	
When (NAME) had loose watery stools, how much liquid did (NAME) receive during the time he/she had a fever. READ RESPONSE CATEGORIES	1=Less 2=ABOUT THE SAME 3=MORE 4=NOTHING TO DRINK 88=don't know
Has (child's name) had refusal to eat/drink in the past 30 d?	1=yes, 2=no, 88=don't know
How many of the past 7 days did the child refuse to eat/drink?	

Figure A.12 Infant morbidity recall module

Question	Outcomes
Enumerator household weight	
Enumerator/infantometer tare weight	
Measurer 1	
Father clothing	1=sweater , 2=jacket, 3=winter scarf, 4=t-shirt; 5=shorts 6=pants, 7=lungi, 97=other
Father height	
Father weight	
Mother's clothing during measurement (mark all that apply)	1=summer saree; 2=winter saree; 3=sweater; 4= jacket; 5= winter scarf; 6=heavy jewelry (bangles); 97=other
Mother height	
Mother mid-upper arm circumference	
Was the infant measured in any clothing?	1=yes; 2= no
Infant clothing during measurement (Mark all that apply)	1=sweater; 2= thick socks; 3= hat; 4= sweat pants; 5=shorts; 6=t-shirt; 7=diaper; 8=blanket; 9= standard study blanket; 97=other
Mother weight	
Infant weight	
Infant head circumference	
Infant calf circumference	
Infant crown-heel length	
Measurer 2	
Father height	
Mother height	
Mother's mid-upper arm circumference	
Infant head circumference	
Infant calf circumference	
Infant crown-heel length	
Is a second measure required for father's height?	1=yes, 2=no
Measurer 1 father height 2	
Measurer 2 father height 2	
Is a second measure required for pregnant woman's height	1=yes, 2=no

Figure A.13 (continued)

Measurer 1 mother height	
Measurer 2 mother height	
Is a second measure required for Mother's MUAC?	
Measurer 1 MUAC 2	
Measurer 2 MUAC 2	
Is a second measure required for head circumference?	1=yes, 2=no
Measurer 1 Infant head circumference 2	
Measurer 2 Infant head circumference 2	
Is a third measure required for head circumference?	1=yes, 2=no
Measurer 1 Newborn head circumference 3	
Measurer 2 Newborn head circumference 3	
Is a second measure required for calf circumference?	1=yes, 2=no
Measurer 1 calf circumference 2	
Measurere 2 calf circumference 2	
Is a third measure required for calf circumference?	
Measurer 1 calf circumference 3	
Measurere 2 calf circumference 3	
Is a second measure required for crown-heel length?	1=yes, 2=no
Measurer 1 crown-heel length 2	
Measurere 2 crown-heel length 2	
Is a third measure required for crown-heel length?	1=yes, 2=no
Measurer 1 crown-heel length 3	
Measurer 2 crown-heel length 3	

Figure A.13 Anthropometry module

Appendix B
Chapter 3

This appendix supplements Chapter 3 and provides additional detail for items referenced in the main text. **Table B.1** shows the unadjusted mean early neonatal weights and lengths by month of conception. **Table B.2** provides information about the mean age of infants at the time of the birth visit measurement.

In the present study, 599 pregnant women were identified across nine villages. Only 225 infants, however, were included in the present analyses. To investigate the potential for selection bias in the final sample, we conducted comparisons on available maternal and household characteristics (missing data were assumed missing at random) for infants who were measured within seven days of birth and those measured between 8-14 days after birth or not measured at the birth visit (**Table B.3**). The only significant differences observed between these two groups was mean maternal mid-upper arm circumference (MUAC; slightly lower in mother's of infants measured within seven days), and in the proportion of infants represented from different study villages. We did not, however, find any strong evidence to suggest that women whose infants were measured within seven days were more likely to be measured because their mother's had lower MUACs. Although some differences in village characteristics (e.g. socio-economic status), were observed, we did not find any indication that the difference in the proportion of infants represented from different study villages resulted in systematic positive or negative bias in estimates of early neonatal size, or potential predictors of early neonatal size. We controlled for village as a fixed effect in the present analyses.

The results from the present study reveal that early neonatal weights (measured within seven days of birth) were significantly lower than the total sample mean only for infants conceived between July and September 2015. To explore whether this significant difference could be an artifact of differential selection bias, we conducted a comparison of available maternal and household characteristics for infants conceived between July and September 2015 and either measured or not measured, and for infants who were born in all other study months and either measured or not measured. We observed a significantly greater proportion of primiparious women in the sample of infants conceived between July and September 2015, and measured within seven days of birth compared to infants who were either measured between 8-14 days after birth or not measured at the birth visit. For infants conceived between July and September 2015, however, we have little data available for the group of infants who were measured between 8-14 days after birth or not measured at the birth visit. For infants conceived in all other study months, the only significant difference observed between the two groups was in the proportion of infants represented from different study villages. We do not have any strong evidence to suggest that the differences in proportion of infants represented from different study villages resulted in systematic positive or negative bias in estimates of early neonatal size, or potential predictors of early neonatal size. Although some differences in village characteristics (socio-economic status) were observed, village was controlled as a fixed effect in the present analyses.

The relationship between postnatal growth and weight was expected to be non-linear. We therefore conducted sensitivity analyses in which alternative specifications of infant postnatal age were included in structural equation models of early neonatal weight as the dependent variable. Neither a quadratic term, nor a categorical age term (0-2 days, 3-5 days and 6-7 days) was significantly associated with early neonatal weight. In addition, a comparison of models controlling for these different age variables, separately, revealed negligible differences in model parameters and model inference. We therefore concluded that controlling for a linear infant age term was an appropriate way to model this relationship (**Table B.5**).

In the present analyses, we assumed missing at random (MAR), for missing data on independent variables. We therefore conducted sensitivity analyses, separately for models of early neonatal weight and length, in which the full information maximum likelihood procedure was not used to handle missing data (analyses conducted only on complete cases) (**Table B.6**; **B.7)**. These alternate model specifications revealed negligible differences in model parameters and model inference. The exception is the slightly less statistical significance observed for the three-month period of conception coefficients. The reason for this difference may be related to the smaller sample size that resulted from only using complete cases. In comparisons of key characteristics for those with and without missing data on independent variables, we observed no significant differences, except for the proportion of infants conceived in different months (results not shown). We did not, however, find any evidence to suggest that this difference in proportions was due to anything other than logistical field constraints. The likelihood of bias is expected to be greater for analyses that exclude subjects with incomplete data on independent variables as compared to the possible bias introduced from falsely assuming MAR.

Our assumption of MAR therefore seems reasonable.

Appendix B figures and tables

Table B.1 Unadjusted mean early neonatal weights and lengths by month of conception in Shivgarh

Conception month	Weight[a]	Length [a]
November 2013	2832 ± 103 (n=5)	49.9 ± 1.2 (n=2)
December 2013	2848 ± 507 (n=22)	48.7 ± 1.9 (n=22)
January 2014	2599 ± 534 (n=26)	48.1 ± 2.2 (n=27)
February 2014	2623 ± 510 (n=21)	47.2 ± 1.6 (n=21)
March 2014	2577 ± 617 (n=17)	47.0 ± 2.6 (n=19)
April 2014	2614 ± 481 (n=11)	47.1 ± 2.1 (n=11)
May 2014	2653 ± 423 (n=20)	47.3 ± 2.0 (n=20)
June 2014	2803 ± 555 (n=9)	47.8 ± 1.9 (n=9)
July 2014	2613 ± 387 (n=6)	47.8 ± 2.4 (n=6)
August 2014	2597 ± 443 (n=3)	47.4 ± 1.1 (n=3)
September 2014	2458 ± 485 (n=13)	47.7± 3.3 (n=12)
October 2014	2802 ± 478 (n=6)	48.3 ± 1.4 (n=6)
November 2014	2818 ± 246 (n=9)	48.0 ± 1.8 (n=9)
December 2014	2638 ± 395 (n=5)	48.3 ± 2.4 (n=5)

[a] Mean ± SD

Table B.2 Age of infants at time of measurement at the birth visit, and percent of sample measured within seven days for three-month periods of birth

Three-month birth period	Age at measurement [a]	% of all infants measured within 14 days
Conceived Nov-Dec 2013 (n=27)	2.6 ± 2.3	82.9
Conceived Jan-Mar 2014 (n=64)	2.5 ± 2.0	83.8
Conceived Apr-Jun 2014 (n=40)	3.4 ± 2.2	69.0
Conceived Jul-Sep 2014 (n=22)	3.5 ± 2.2	75.9
Conceived Oct-Dec 2014 (n=20)	3.7 ± 2.1	76.9
Overall sample	3.0 ± 2.0	72.8

[a] Mean ± SD

Table B.3 Comparison of key characteristics (mean ± SD or N (%)) of mothers and households of infants measured within seven days of birth and those measured between 8-14 days after birth or not measured at the birth visit

Characteristics	Measured within seven days of birth (n=225)	Measured within 8-14 days after birth or not measured at birth visit (n=374)
Maternal characteristics		
Height, cm	149.9± 5.3 (n=180)	150.0 ± 4.9 (n=225)
Attained 3rd trimester weight,kg	50 ± 8.0 (n=178)	51 ± 7.0 (n=224)
Mid-upper arm circumference, cm*	23.2 ± 2.2 (n=222)	23.6± 2.3 (n=224)
Maternal age, y	25.5 ± 5.0 (n=221)	25.4 ± 4.6 (n=316)
Parity	2.79 ± 2.0(n=200)	1.8 ± 1.4 (n=329)
Primiparous (N (%))	56 (28.0)	198(60.2)
Socio-demographic characteristics		
Never went to school (N (%))	146 (66.1)	315 (36.2)
Socio-economic class (N (%))	(n=208)	(n=344)
Low SES	70 (33.7)	114 (33.1)
Middle SES	68 (32.7)	117 (34.0)
High SES	70 (33.7)	113 (32.9)
Household food insecurity score	1.18 ± 2.09 (n=218)	1.04 ± 2.26 (n=312)
Food insecure (N (%))	74 (33.9)	102 (32.7)
Village* (N (%))		n=375
Village 1	30 (13.3)	28 (7.5)
Village 2	32 (14.2)	69 (18.4)
Village 3	22 (9.8)	41(10.9)
Village 4	37 (16.4)	57(15.2)
Village 5	30 (13.3)	55(14.7)
Village 6	5 (2.2)	29 (7.7)
Village 7	14 (6.2)	30 (8.0)
Village 8	34 (15.1)	35 (9.3)
Village 9	21 (9.3)	31 (8.3)
Three-month conception periods	(n=178)	(n=56)
Conceived Nov–Dec 2013(n=29)	29 (16.3)	7 (12.5)
Conceived Jan-Mar 2014 (n=67)	67 (37.6)	14 (25.0)
Conceived Apr-Jun 2014 (n=40)	40 (22.5)	18 (32.1)
Conceived Jul-Sep 2014 (n=22)	22 (12.4)	19.6 (10.7)
Conceived Oct-Dec 2014 (n=20)	20 (11.2)	6 (10.7)

P-values are based on t-test for continuous variables and chi-squared for categorical variables
* Groups significantly different ($p<0.05$)

Table B.4 Comparison of key characteristics (mean ± SD or N (%)) for infants conceived between July and September 2014 and either measured or not measured, and for infants born in all other study months that were either measured or not measured

	Conceived July-September 2014		**Conceived in all other three-month periods (November-December 2013; January-March 2014; April-June 2014; October-December 2014)**	
Characteristics	Measured within seven days of birth	Measured within 8-14 days after birth or not measured at birth	Measured within seven days of birth	Measured within 8-14 days after birth or not measured at birth
Maternal Characteristics				
Height, cm	150.5 ± 4.2 (n=19)	150 ± 4.3 (n=10)	149.8 ± 5.1 (n=135)	149.5 ± 4.9 (n=41)
Attained 3rd trimester weight, kg	50 ± 6 (n=19)	51.3 ± 9.9 (n=10)	49 ± 7 (n=133)	51 ± 8 (n=41)
Mid-upper arm circumference, cm +	23.4 ± 1.2 (n=19)	23.6 ± 2.5 (n=10)	23.0 ± 2.3 (n=134)	23.9 ± 2.8 (n=41)
Maternal age, y	25.0 ± 5.3 (n=22)	25.8 ± 5.3 (n=11)	25.6 ± 5.3 (n=154)	25.5 ± 5.1 (n=45)
Parity	1.8 ± 1.4 (n=22)	2.4 ± 1.2 (n=9)	2.1 ± 1.8 (n=140)	1.7 ± 1.3 (n=42)
Primiparous*	16 (72.7)	3 (33.3)	72 (51.4)	27 (64.3)
Socio-demographic characteristics				
Education	(n=22)	(n=10)	(n=154)	(n=45)
Never went to school	6 (27.3)	4 (0.4)	50 (32.5)	32 (71.1)
Socio-economic status	(n=21)	(n=10)	(n=197)	(n=45)
Low SES	7 (31.82)	4 (40.0)	46 (31.3)	15 (33.3)
Middle SES	10(45.45)	5 (50.0)	48 (32.7)	17 (37.8)
High SES	5 (22.73)	1(10.0)	53 (36.1)	13 (28.9)
Food Insecurity Score	0.70 ± 1.22 (n=20)	1.60 ± 4.72 (n=10)	1.31 ± 2.27 (n=153)	1.27 ± 2.82 (n=44)
Food insecure (N (%))	5 (25.0)	2 (20.0)	56 (36.6)	16 (36.4)
Village+		(n=11)		(n=45)
Village 1	0 (0)	1 (9.1)	26 (16. 7)	7(15.6)
Village 2	6 (27.3)	1(9.1)	21(13.5)	4 (8.9)
Village 3	2 (9.1)	1 (9.1)	16 (10.3)	5 (11.1)
Village 4	6 (27.3)	2 (18.2)	23(14.7)	10(22.2)
Village 5	6 (27.3)	1 (9.1)	15(9.6)	4 (8.9)
Village 6	0 (0)	2 (18.2)	2 (1.3	6 (13.3)
Village 7	0 (0)	1 (9.1)	11(7.1)	5(11.1)
Village 8	2 (9.1)	2 (18.2)	27(17.3)	3 (6.7)
Village 9	1 (4.17)	2 (4.4)	15 (9.6)	1(2.2)

P-values are based on t-test for continuous variables and chi-squared for categorical variables

* Infants conceived between July and September 2014 and measured within seven days of birth were significantly different (p <0.05) than those not measured within seven days of birth

\+ Infants conceived in all other three-month clusters and measured within seven days of birth were significantly different (p <0.05) than those not measured within seven days of birth

Table B.5 Association of maternal[a] and infant[b] variables and three-month periods of conception with mean early neonatal weights (g) using structural equation modeling and full-information-maximum-likelihood to handle missing data in independent variables and alternate specifications of infant age[c]. Models 1a, 2a and Final model a include food insecurity

Independent Variables	Model 1[d] (n=220)	Model 1a.[days] (n=220)	Model 2[d] (n=220)	Model 2a[d]. (n=220)	Final model [d] (n=220)	Final model a[d] (n=220)
Infant postnatal age, d	23.1 ± 50.7 p=0.65	28.5 ± 49.9 p=0.57	---	---	-3.9 ± 14.3 p=0.79	-1.3 ± 14.2 p=0.93
Infant postnatal age^2, d	-4.0 ± 7.1 p=0.57	-4.4 ± 7.0 p=0.53	---	---	---	---
0-2, d	---	---	Ref	Ref	---	---
3-5, d	---	---	40.7± 64.6 p=0.53	55.9 ± 63.7 p=0.38	---	---
6-7, d	---	---	-32.5± 88.0 p=0.712	-28.8 ± 86.6 p=0.74	---	---
Gestational age, wk	62.4 ± 23.0 p=0.007	60.6 ± 22.7 p=0.008	63.9± 22.4 p=0.004	62.8± 22.1 p=0.004	63.9± 22.4 p=0.004	62.8 ± 22.1 p=0.004
Male	Ref	Ref	Ref	Ref	Ref	Ref
Female	-200.8 ± 58.2 p=0.001	-230.3 ± 58.2 p<0.001	-198.5 ± 58.6 p=0.001	-227.0 ± 58.4 p<0.001	-206.1 ± 58.2 p<0.001	-235.5 ± 58.3 p<0.001

Table B.5 (continued)

Maternal height, cm	30.0 ± 5.7 p<0.001	28.5 ± 5.7 p<0.001	29.7 ± 5.7 p<0.001	28.2 ± 5.6 p<0.001	30.3 ± 5.7 p<0.001	28.9 ± 5.7 p<0.001
Multiparous	Ref	Ref	Ref	Ref	Ref	Ref
Primiparous	-281.2 ± 70.8 p<0.001	-305.3 ± 70.1 p<0.001	-274.6 ± 70.8 p<0.001	-299.5 ± 69.9 p<0.001	-283.0 ± 70.5 p<0.001	-307.8 ± 69.8 p<0.001
Any education	Ref	Ref	Ref	Ref	Ref	Ref
No education	-152.3 ± 66.3 p=0.022	-175.4 ± 65.6 p=0.008	-153.0± 66.1 p=0.021	-177.6± 65.3 p=0.006	-150.7± 66.3 p=0.023	-173.2 ± 65.5 p=0.008
Food secure	---	Ref	---	Ref	---	Ref
Food insecure	---	-182.7 ± 66.0 p=0.006	---	-189.9± 65.6 p=0.004	---	-181.8± 66.0 p=0.006
Conceived Nov–Dec 2013	Ref	Ref	Ref	Ref	Ref	Ref
Conceived Jan-Mar 2014	-145.6 ± 97.5 p=0.135	-153.5 ± 96.5 p=0.112	-139.1 ± 96.5 p=0.149	-143.1 ± 95.2 p=0.133	-141.4 ± 96.9 p=0.14	-147.4 ± 95.9 p=0.12
Conceived Apr-Jun 2014	-75.1 ± 105.0 p=0.47	-61.9 ± 104.2 p=0.55	-69.9 ±103.2 p=0.50	-50.7± 102.2 p=0.62	-71.1 ± 104.6 p=0.50	-56.4 ± 103.8 p=0.59
Conceived Jul-Sep 2014	-292.6 ± 124.2 p=0.019	-319.2 ± 122.7 p=0.009	-283.4 ±122.5 p=0.021	-303.7±120.7 p=0 .012	-289.3 ±123.8 p=0.019	-313.7 ± 122.3 p=0.010
Conceived Oct-Dec 2014	-17.1 ± 26.1 p=0.89	-25.5 ± 125.1 p=0.84	-9.5 ± 124.2 p=0.94	-11.9 ± 122.8 p=0.92	-13.6 ±126.1 p=0.91	-20.6± 125.1 p=0.87
R^2	0.33	0.35	0.33	0.36	0.33	0.35

[a] Maternal variables include height, parity and education
[b] Infant variables include postnatal age, gestational age, sex
[c]All models control for village as a fixed effect
[d] Coefficient ± SE

Table B.6 Association of maternal[a] and infant[b] variables and three-month periods of conception with early neonatal weight (g) using structural equation modeling without using the full-information-maximum-likelihood procedure to handle missing data in independent variables.[c] Models 1a and Final model a include food insecurity

Independent Variables	Model 1[d] (n=154)	Model 1a[d] (n=150)	Final model [d] (n=220)	Final modela[d] (n=220)
Infant post-natal age, d	-4.6 ± 17.1 p=0.79	-7.1 ± 17.8 p=0.69	-3.9 ± 14.3 p=0.79	-1.3 ± 14.2 p=0.93
Gestational Age, wk	61.7 ± 23.6 p= 0.009	64.4 ± 23.1 p=0.005	63.9 ± 22.4 p=0.004	62.8 ± 22.1 p=0.004
Male	Ref	Ref	Ref	Ref
Female	-198.7 ± 68.3 p=0.004	-245.7 ± 67.6 p<0.001	-206.1± 58.2 p<0.001	-235.5 ± 58.3 p<0.001
Maternal height, cm	27.0 ± 6.7 p<0.001	27.4 ± 7.0 p=0.000	30.3± 5.7 p<0.001	28.9 ± 5.7 p<0.001
Multiparous	Ref	Ref	Ref	Ref
Primiparous	-259.1 ± 78.4 p=0.001	-309.7± 78.0 p<0.001	-283.0 ± 70.5 p<0.001	-307.8 ± 69.8 p<0.001
Any education	Ref	Ref	Ref	Ref
No education	-132.7 ± 77.5 p=0.087	-163.0 ± 76.9 p=0.034	-150.7± 66.3 p=0.023	-173.2 ± 65.5 p=0.008
Food Secure	---	Ref	---	Ref
Food Insecure	---	-205.0 ± 73.0 p=0.005	---	-181.8 ± 66.0 p=0.006
Conceived Nov–Dec 2013	Ref	Ref	Ref	Ref
Conceived Jan-Mar 2014	-101.9 ± 104.4 p=0.33	-71.9 ± 106.4 p=0.50	-141.4 ± 96.9 p=0.14	-147.4 ± 95.9 p=0.12
Conceived Apr-Jun 2014	-53.3 ± 111.1 p=0.63	-11.1 ± 115.1 p=0.92	-71.1 ± 104.6 p=0.50	-56.4 ± 103.8 p=0.59
Conceived Jul-Sep 2014	-228.1 ± 129.1 p=0.077	-193.0 ± 130.7 p= 0.140	-289.3 ± 123.8 p=0.019	-313.7 ± 122.3 p=0.010
Conceived Oct-Dec 2014	35.3± 149.3 p=0.81	64.0 ± 147.8 p=0.67	-13.6 ± 126.1 p=0.91	-20.6± 125.1 p=0.87
R^2	0.28	0.34	0.33	0.35

[a] Maternal variables include height, parity and education
[b] Infant variables include postnatal age, gestational age, sex
[c]All models control for village as a fixed effect
[d] Coefficient ± SE

Table B.7 Association of maternal[a] and infant[b] variables and three-month periods of conception with early neonatal length (cm) using structural equation modeling without using the full-information-maximum-likelihood procedure to handle missing data in independent variables.[c] Models 1a and Final model a include food insecurity

Independent Variables	Model 1 [d] (n=157)	Model 1a [d] (n=153)	Final model [d] (n=222)	Final model a [d] (n=222)
Infant post-natal age, d	0.18 ± 0.077 p=0.023	0.17 ± 0.08 p=0.034	0.16 ± 0.07 p= 0.014	0.17 ± 0.06 p=0.007
Gestational Age, wk	0.24 ± 0.11 p=0.030	0.26 ± 0.11 p=0.015	0.24 ± 0.10 p=0.020	0.24 ± 0.10 p=0.022
Male	Ref	Ref	Ref	Ref
Female	-0.51 ± 0.31 p=0.102	-0.72 ± 0.31 p=0.019	-0.59 ± 0.27 p=0.028	-0.74 ± 0.27 p=0.006
Maternal height, cm	0.13 ± 0.03 p=0.000	0.13± 0.03 p=0.000	0. 12 ± 0.026 p<0.001	0.12 ± 0.03 p<0.001
Multiparous	Ref	Ref	Ref	Ref
Primiparous	-0.99 ± 0.35 p= 0.005	-1.25 ± 0.35 p<0.001	-1.05 ± 0.32 p=0.001	-1.17 ± 0.31 p<0.001
Any education	Ref	Ref	Ref	Ref
No education	-0.19 ± 0.35 p=0.578	-0.27 ± 0.34 p=0.43	-0.34 ± 0.30 p=0.26	-0.45 ± 0.29 p=0.122
Food Secure	---	Ref	---	Ref
Food insecure	---	-0.90 ± 0.34 p=0.008	---	-0.88 ± 0 0.30 p=0.004
Conceived Nov–Dec 2013	Ref	Ref	Ref	Ref
Conceived Jan-Mar 2014	-0.78 ± 0.48 p=0.105	-0.60 ± 0.49 p=0.215	-1.04 ± 0.45 p=0.022	-1.06 ± 0.45 p=0.018
Conceived Apr-Jun 2014	-1.35 ± 0.52 p=0.009	-1.15 ± 0.53 p=0.029	-1.58 ± 0.49 p=0.001	-1.50 ± 0.48 p= 0.002
Conceived Jul-Sep 2014	-1.15 ± 0.60 p=0.054	-0.88 ± 0.60 p=0.14	-1.43 ± 0.59 p=0.015	-1.53 ± 0.58 p=0.008
Conceived Oct-Dec 2014	-0.24± 0.70 p=0.73	-0.06 ± 0.69 p=0.93	-0.52 ± 0.60 p=0.38	-0.53 ± 0.59 p=0.37
R^2	0.28	0.32	0.28	0.31

[a] Maternal variables include height, parity and education
[b] Infant variables include postnatal age, gestational age, sex
[c]All models control for village as a fixed effect
[d] Coefficient ± SE

Appendix C
Chapter 4

These appendices present additional details for statistical analyses not presented in the main text of Chapter 4. **Figure C.1** provides sample code for Stata's mixed procedure used to generate rates of growth in weight for the 3-6 month age interval. **Table C.1** and **Table C.2** show the results of the regression models of weight and length velocity, respectively, in each of the four-age intervals of growth. Month at the start of the growth interval and infant sex were considered as covariates. Stata's *lincom* procedure was used to for post-estimation comparisons following these regression models and is presented in the main text.

Appendix C figures and tables

```
mixed weight age if age >=2.5 & age < 6.5 || id: age, cov(unstructured) stddev
estimates store rc
predict ebsweight36 ebiweight36, reffects
collapse (mean) ebsweight36 ebiweight36, by(id)
```

Figure C.1 Example code for generating individual level weight slopes for infants in the 3-6 month age interval[12]

[12] weight=infant weight(g); age= age of the infant in months;ebsweight36= weight slopes for infants in the 3-6 month interval; ebiweight36= weight intercepts for infants in the 3-6 month interval; id=unique individual level infant identification number

Table C.1 Association of month at the start of the growth interval and infant sex with weight velocity in each of the four-three month age intervals

Independent variables	Weight Velocity 0-3 m [a] (n=339)	Weight Velocity 1-4 m [a] (n=332)	Weight Velocity 2-5 m [a] (n=316)	Weight Velocity 3-6 m [a] (n=286)
Male	Ref	Ref	Ref	Ref
Female	-74 ± 14 (p<0.001)	-57 ± 10 (p<0.001)	-56 ± 9 (p<0.001)	-47 ± 11 (p<0.001)
August 2014	Ref	---	---	---
September 2014	-2 ± 40 (p=0.97)	Ref	---	---
October 2014	-57 ± 39 (p=0.14)	-3 ± 30 (p=0.91)	Ref	---
November 2014	-58 ± 39 (p=0.14)	-18 ± 30 (p=0.54)	2 ± 29 (p=0.95)	Ref
December 2014	-37 ± 40 (p=0.35)	-23 ± 29 (p=0.43)	2 ± 29 (p=0.96)	12 ± 40 (p=0.77)
January 2015	-39 ± 40 (p=0.33)	-22 ± 30 (p=0.47)	17 ±28 (p=0.55)	56 ± 45 (p=0.21)
February 2015	-22 ± 38 (p=0.58)	-32 ± 30 (p=0.29)	7 ± 29 (p=0.82)	7 ± 36 (p=0.85)
March 2015	-18 ± 41 (p=0.66)	-35± 29 (p=0.22)	-4 ± 29 (p=0.89)	-10 ± 36 (p=0.79)
April 2015	2 ± 45 (p=0.96)	-13 ± 31 (p=0.68)	3 ± 28 (p=0.91)	-3 ± 36 (p=0.93)
May 2015	-21± 48 (p=0.66)	-32 ± 34 (p=0.33)	8 ± 30 (p=0.79)	38 ± 36 (p=0.29)
June 2015	-11± 43 (p=0.80)	19 ± 35 (p=0.58)	2 ± 32 (p=0.95)	9 ± 37 (p=0.80)
July 2015	2± 49 (p=0.96)	-24 ± 31 (p=0.44)	17 ± 34 (p=0.61)	29 ± 39 (p=0.46)
August 2015	-37 ± 40 (p=0.35)	-12 ± 36 (p=0.73)	-12 ± 29 (p=0.68)	27 ± 40 (p=0.50)
September 2015	-10 ± 45 (p=0.83)	-21± 29 (p=0.48)	24 ± 33 (p=0.48)	36 ± 36 (p=0.33)
October 2015	15 ± 47 (p=0.76)	-1± 33 (p=0.98)	21 ± 29 (p=0.45)	32 ± 40 (p=0.43)
November 2015	---	6± 35 (p=0.87)	13 ± 32 (p=0.68)	41 ± 36 (p=0.25)
December 2015	---	---	33 ± 33 (p=0.32)	44 ± 39 (p=0.26)
January 2016	---	---	---	45 ± 40 (p=0.27)
R^2	0.10	0.11	0.12	0.11

[a] Coefficient ± SE

Table C.2 Association of month at the start of the growth interval and infant sex with length velocity in each of the four- three-month age intervals

	Length Velocity 0-3 m [a] (n=341)	Length Velocity 1-4 m [a] (n=330)	Length Velocity 2-5 m [a] (n=317)	Length Velocity 3-6 m [a] (n=283)
Male	Ref	Ref	Ref	Ref
Female	-0.090 ± 0.015 (p<0.001)	-0.016 ± 0.012 (p=0.175)	-0.051 ± 0.022 (p=0.023)	-0.074 ± 0.022 (p=0.001)
August 2014	Ref	---	---	---
September 2014	-0.090 ± 0.015 (p=0.72)	Ref	---	---
October 2014	-0.045 ± 0.043 (p=0.29)	0.013 ± 0.036 (p=0.73)	Ref	---
November 2014	-0.062 ± 0.043 (p=0.15)	0.041± 0.036 (p=0.26)	0.022 ± 0.070 (p=0.75)	Ref
December 2014	-0.003 ± 0.044 (p=0.95)	0.059 ± 0.035 (p=0.10)	0.043 ± 0.070 (p=0.53)	-0.023 ± 0.084 (p=0.79)
January 2015	-0.014 ± 0.044 (p=0.75)	0.060 ± 0.036 (p=0.10)	0.069 ± 0.067 (p=0.31)	0.037 ± 0.097 (p=0.70)
February 2015	0.013 ± 0.042 (p=0.77)	0.025 ± 0.036 (p=0.50)	0.121 ± 0.068 (p=0.08)	-0.065 ± 0.077 (p=0.40)
March 2015	0.061 ± 0.045 (p=0.18)	0.045 ± 0.035 (p=0.20)	0.062 ± 0.070 (p=0.372)	0.011 ± 0.077 (p=0.89)
April 2015	0.009 ± 0.049 (p=0.85)	0.044 ± 0.037 (p=0.23)	0.051 ± 0.067 (p=0.44)	-0.055 ± 0.077 (p=0.48)
May 2015	0.043 ± 0.053 (p=0.42)	-0.011 ± 0.040 (p=0.79)	0.130 ± 0.070 (p=0.07)	-0.042 ± 0.077 (p=0.58)
June 2015	0.064 ± 0.048 (p=0.18)	0.097 ± 0.042 (p=0.02)	0.020 ± 0.075 (p=0.79)	-0.044 ± 0.079 (p=0.58)
July 2015	-0.056± 0.055 (p=0.31)	-0.002 ± 0.037 (p=0.96)	-0.028 ± 0.080 (p=0.73)	0.006 ± 0.082 (p=0.95)
August 2015	-0.071 ± 0.044 (p=0.10)	-0.056 ± 0.043 (p=0.19)	-0.017 ± 0.070 (p=0.81)	-0.119 ± 0.085 (p=0.16)
September 2015	-.011 ± 0.049 (p=0.83)	-0.041 ± 0.035 (p=0.25)	-0.056 ± 0.079 (p=0.48)	-0.043 ± 0.078 (p=0.58)
October 2015	-0.015 ± 0.052 (p=0.78)	-0.039 ± 0.040 (p=0.32)	-0.007 ± 0.068 (p=0.92)	0.00008 ± 0.085 (p=0.10)
November 2015	---	0.017 ± 0.042 (p=0.69)	0.025 ± 0.075 (p=0.74)	-0.048 ± 0.077 (p=0.53)
December 2015	---	---	0.120 ± 0.079 (p=0.13)	0.0166 ± 0.082 (p=0.84)
January 2016	---	---	---	0.071 ± 0.085 (p=0.41)
R^2	0.16	0.12	0.08	0.09

[a] Coefficient ± SE

Appendix D
Chapter 5

These appendices present additional details for statistical analyses not presented in the main text of Chapter 5. To test whether the monthly differences in length velocity observed in the 1-4 growth interval was mediated by maternal (food insecurity, diet diversity, maternal morbidity, time spent in agriculture and time spent in childcare) and infant (morbidity, feeding) determinants of undernutrition, we employed the *Difference Method* for mediation analyses [168]. Regression models were constructed using Structural equation modeling (SEM) in Stata. The full information maximum likelihood procedure within SEM was used to handle missing data under the assumption that missing data on covariates were missing at random (MAR) (**Table D.1**). In all models, length velocity in the 1-4 month growth interval was considered as the dependent variable. In model 1, potentially confounding variables were added to a model that included the variables representing the months starting the interval of growth. Models 2-9 show models in which each potential mediator was added, separately, to Model 1. To test for mediation, we calculated the difference between the month coefficients in Model 1 and the month coefficients in each of the models that included potential mediators. Differences were shown to be negligible (not biologically meaningful), and thus a formal significance test of this difference was not conducted. Based on these analyses, we concluded that these individual maternal and child risk factors did not mediate the observed seasonal differences in length velocity in the 1-4 month growth interval.

Figure D.2 and **Figure D.3** present the results of sensitivity analyses that compared the results of regression models with weight and length velocity as the dependent variables, respectively, with and without the implementation the full information maximum likelihood procedure to handle missing data on covariates.

Appendix D figures and tables

Table D.1 Test of mediation of the association of length velocity (cm/mo) in the 1-4 month growth interval and month of the start of the growth interval, maternal[a] and infant[b] variables using structural equation modeling. Numbers in italics represent the difference in coefficients from Model 1

Variables	Model 1: potential mediators not included	Model 2: includes maternal weight velocity	Model 3: includes food insecurity	Model 4: includes diet diversity	Model 5: includes maternal morbidity	Model 6: includes time spent in agriculture	Model 7: includes time spent in childcare	Model 8: includes breastfeeding	Model 9: includes infant morbidity
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	-0.031± 0.011 p=0.006	-0.034 ± 0.011 p=0.003	-0.031 ± 0.011 p=0.006	-0.031 ± 0.011 p=0.006	-0.031 ± 0.011 p=0.005	-0.030 ± 0.011 p=0.008	-0.030± 0.011 p=0.007	-0.032±0.011 p=0.005	-0.031± 0.011 p=0.005
Newborn length, cm	-0.021± 0.003 p<0.001	-0.022± 0.003 p=0.000	0.021± 0.003 p<0.001	-0.021± 0.003 p<0.001	-0.021± 0.003 p<0.001	-0.021± 0.003 p<0.001	-0.022± 0.003 p<0.001	-0.021± 0.003 p<0.001	-0.021± 0.003 p<0.001
Height, cm	0.004 ± 0.001 p=0.001	0.004 ± 0.001 p<0.001	0.004 ± 0.001 p=0.001	0.004 ± 0.001 p=0.001	0.004± 0.001 p=0.001	0.004 ± 0.001 p=0.001	0.004± 0.001 p= 0.001	0.004 ± 0.001 p=0.001	0.004 ± 0.001 p=0.001
Lower class	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Middle class	-0.024 ± 0.015 p=0.111	-0.026 ± 0.015 p=0.085	-0.022 ± 0.016 p=0.175	-0.026 ± 0.016 p=0.100	-0.024 ± 0.015 p=0.116	-.024 ± 0.015 p=0.111	-0.024 ± 0.015 p=0.109	-0.023 ± 0.015 p=0.127	- 0.025± 0.015 p=0.109
Upper class	-0.015 ± 0.015 p=0.33	-0.016 ± 0.015 p=0.31	-0.022 ± 0.016 p=0.175	-0.017 ± 0.016 p= 0.29	-0.015 ± 0.015 p=0.33	-0.015 ± 0.015 p=0.33	-0.014 ± 0.015 p=0.354	-0.011± 0.016 p=0.47	-0.015 ± 0.015 p=0.32
Aug 2014	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Sep 2014	-0.013 ± 0.034 p=0.69	-0.023 ± 0.034 p=0.50 *0.010*	-0.006 ± 0.034 p=0.86 *-0.007*	-0.014 ± 0.034 p=0.68 *0.001*	-0.008 ± 0.034 p=0.81 *-0.005*	-0.013 ± 0.034 p=0.690 *0.000*	-0.014 ± 0.034 p=0.69 *0.001*	-0.016 ± 0.034 p=0.64 *0.003*	-0.012 ± 0.034 p=0.72 *-0.001*
Oct 2014	0.029 ± 0.034 p=0.38	0.019 ± 0.034 p=0.58 *0.010*	0.037 ± 0.034 p=0.272 *-0.008*	0.029 ± 0.034 p=0.397 *0.000*	0.033 ± 0.034 p=0.33 *-0.004*	0.030 ± 0.034 p=0.377 *-0.001*	0.032 ± 0.034 p=0.34 *-0.003*	0.029 ± 0.034 p=0.39 *0.000*	0.030 ± 0.034 p=0.37 *-0.001*

Table D.1 (continued)

Nov 2014	0.055 ± 0.033 p=0.099	0.046 ± 0.033 p=0.165 *0.009*	0.063± 0.033 p=0.059 *-0.008*	0.054 ± 0.033 p=0.100 *0.001*	0.059 ± 0.034 p=0.079 *-0.004*	0.056 ± 0.033 p=0.090 *-0.001*	0.055 ± 0.033 p=0.093 *0.000*	0.051± 0.033 p=0.122 *0.004*	0.054 ± 0.033 p=0.101 *0.001*
Dec 2014	0.032 ± 0.034 p=0.34	0.023 ± 0.034 p= 0.499 *0.009*	0.042 ± 0.034 p=0.22 *-0.010*	0.032 ± 0.034 p=0.35 *0.000*	0.037 ± 0.034 p=0.29 *-0.005*	0.031 ± 0.034 p=0.36 *0.001*	0.033 ± 0.034 p=0.33 *-0.001*	0.032 ± 0.034 p=0.34 *0.000*	0.034 ± 0.034 p=0.32 *-0.002*
Jan 2015	-0.007 ± 0.035 p=0.84	-0.010 ± 0.035 p=0.767 *0.003*	0.001± 0.035 p=0.97 *-0.008*	-0.008 ± 0.035 p=0.83 *0.001*	-0.003 ± 0.035 p=0.94 *-0.004*	-0.007 ± 0.035 p=0.85 *0.000*	-0.007 ± 0.035 p=0.85 *0.000*	-0.003± 0.035 p=0.93 *-0.004*	-0.005 ± 0.035 p=0.88 *-0.002*
Feb 2015	0.020 ± 0.033 p=0.54	0.021± 0.033 p=0.52 *-0.001*	0.029 ± 0.033 p=0.38 *-0.009*	0.020 ± 0.033 p=0.54 *0.000*	0.023 ± 0.033 p=0.48 *-0.003*	0.021± 0.033 p=0.52 *-0.001*	0.020 ± 0.033 p=0.55 *0.000*	0.019 ± 0.033 p=0.56 *0.001*	0.022 ± 0.033 p=0.51 *-0.002*
Mar 2015	0.026 ± 0.035 *p=0.47*	0.020 ± 0.035 p=0.57 *0.006*	0.037 ± 0.036 p=0.31 *-0.011*	0.025 ± 0.035 p=0.48 *0.001*	0.031± 0.036 p=0.39 *-0.005*	0.024 ± 0.035 p=0.49 *0.002*	0.028 ± 0.035 p=0.43 *-0.002*	0.023± 0.036 p=0.52 *0.003*	0.025 ± 0.035 p=0.48 *0.001*
Apr 2015	-0.000 ± 0.039 p=0.99	0.002± 0.039 p=0.97 *-0.002*	0.005 ± 0.034 p=0.89 *-0.006*	-0.001 ± 0.039 p=0.99 *0.000*	0.004 ± 0.039 p=0.92 *-0.004*	-0.004 ± 0.039 p=0.92 *0.004*	-0.002 ± 0.039 p=0.96 *0.002*	-0.001± 0.039 p=0.97 *0.001*	0.003 ± 0.039 p=0.94 *-0.003*
May 2015	0.079 ± 0.041 p=0.055	0.078 ± 0.041 p=0.057 *0.001*	0.085 ± 0.041 p=0.039 *-0.006*	0.079 ± 0.041 p=0.058 *0.000*	0.082 ± 0.042 p=0.048 *-0.003*	0.077 ± 0.041 p=0.061 *0.002*	0.079 ± 0.041 p=0.055 *0.000*	0.080 ± 0.041 p=0.051 *-0.001*	0.078 ± 0.041 p=0.059 *0.001*

Table D.1 (continued)

Jun 2015	-0.023 ±0.035 p=0.52	-0.025 ±0.035 p=0.48 *0.002*	-0.013 ±0.036 p=0.71 *-0.010*	-0.023 ±0.035 p=0.51 *0.000*	-0.012 ±0.034 p=0.61 *-0.005*	-0.022 ±0.035 p=0.53 *-0.001*	-0.020 ±0.035 p=0.56 *-0.003*	-0.024 ±0.035 p=0.50 *0.001*	-0.023± 0.035 p=0.50 *0.000*
Jul 2015	-0.035 ±0.043 p=0.42	-0.034±0.043 p=0.43 *-0.001*	-0.032±0.043 p=0.46 *-0.003*	-0.034±0.043 p=0.427 *-0.001*	-0.030± 0.043 p=0.497 *-0.005*	-0.037±0.043 p=0.39 *0.002*	-0.033 ±0.043 p=0.44 *-0.002*	-0.031 ±0.043 p=0.47 *-0.004*	-0.035± 0.043 p=0.41 *0.000*
Aug 2015	-0.038 ±0.034 p=0.26	-0.042± 0.034 p= 0.21 *0.004*	-0.032 ±0.034 p=0.35 *-0.006*	-0.040± 0.034 p=0.25 *0.002*	-0.040± 0.034 p=0.25 *0.002*	-0.041±0.034 p=0.23 *0.003*	-0.039 ±0.034 p=0.25 *0.001*	-0.045± 0.03 p=0.19 *0.007*	-0.036± 0.034 p=0.28 *-0.002*
Sep 2015	-0.056 ±0.038 p=0.135	-0.059± 0.038 p=0.120 *0.003*	-0.049± 0.038 p=0.20 *-0.007*	-0.057± 0.038 p=0.13 *0.001*	-0.053± 0.038 p=0.16 *-0.003*	-0.057± 0.038 p=0.13 *0.001*	-0.057± 0.038 p=0.131 *0.001*	-0.059± 0.038 p=0.115 *0.003*	-0.054± 0.038 p=0.15 *-0.002*
Oct 2015	-0.013±0.041 p=0.75	-0.027± 0.042 p=0.53 *0.014*	-0.006 ±0.042 p=0.88 *-0.007*	-0.013±0.041 p=0.75 *0.000*	-0.011±0.042 p=0.80 *-0.002*	-0.016±0.041 p=0.695 *0.003*	-0.020±0.042 p= 0.64 *0.007*	-0.014 ±0.041 p= 0.74 *0.001*	-0.010 ±0.041 p=0.80 *-0.003*
Continuous mediator	---	0.016± 0.009 p=0.072	0.005 ± 0.003 p=0.18	-0.000 ±0.006 p= 0.96	0.002 ±0.002 p=0.32	-0.000±0.000 p=0.29	0.000±0.000 p=0.33	---	-0.000±0.000 p=0.56
Exclusively breastfed entire interval	---	---	---	---	---	---	---	Ref	---
Exclusively breastfed part of interval	---	---	---	---	---	---	---	-0.027±0.017 p=0.110	---
Not exclusively breastfed in interval	---	---	---	---	---	---	---	-0.015±0.014 p=0.27	---

[a] Maternal variables include height, socio-economic status and height

[b] Infant variables include newborn length and sex

Table D.2 Association of fixed time-invariant[a] maternal and infant variables and maternal postpartum and infant postnatal[b] variables with length velocity in the 1-4 month growth interval (cm/mo) using structural equation modeling[c] with and without the implementation of the full information maximum likelihood procedure

Variables	Model 1[d,e] (n=172)	Model 4[d,f] (n=330)
Female	-0.039 ± 0.014 p=0.004	-0.039 ± 0.011 p=0.001
Male	Ref	Ref
Newborn length, cm	-0.017 ± 0.003 p<0.001	-0.022 ± 0.003 p<0.001
Starts growth interval in higher risk season (Aug-Oct 2015)	0.442 ± 0.138 p=0.001	0.204 ± 0.115 p=0.076
Starts growth in lower risk season (all other months)	Ref	Ref
Maternal height, cm	0.001 ± 0.001 p=0.29	0.004 ± 0.001 p=0.005
Exclusively breastfed	0.012 ± 0.014 p=0.38	0.022 ± 0.012 p= 0.065
Not exclusively breastfed	Ref	Ref
Received any vaccines	-0.056 ± 0.033 p=0.085	-0.061 ± 0.026 p=0.020
Received no vaccines	Ref	Ref
Child morbidity	-0.014 ± 0.004 p=0.001	-0.012 ± 0.003 p<0.001
Childcare, min/d	0.00006 ± 0.00009 p=0.47	0.00004 ± 0.00007 p=0.57
Higher agriculture tertile	-0.034 ± 0.015 p=0.026	-0.019 ± 0.013 p=0.15
Middle agriculture tertile	-0.045±0.019 p=0.018	-0.037 ± 0.017 p=0.027
Lower agriculture tertile	Ref	Ref
Maternal morbidity	0.0039 ± 0.002 p=0.073	0.003 ± 0.002 p=0.081
High risk season * childcare	-0.0014 ± 0.0004 p<0.001	-0.0007 ± 0.0003 p=0.019
Child morbidity* vaccination	0.012 ± 0.004 p=0.008	0.012 ± 0.003 p=0.001
R^2	0.37	0.32

[a] Maternal and infant prenatal variables include maternal height, parity, infant sex, gestational age and early neonatal length

[b] Maternal postpartum variables include morbidity, food security, diet diversity, weight velocity, and agricultural work; Infant postnatal variables include month starting the growth interval, morbidity, breastfeeding, vaccination and childcare

[c] All models control for village as a fixed effect

[d] Mean ± SE

[e] Model 1 considers maternal and infant prenatal variables, season starting growth interval and interactions and does not implement the full information maximum likelihood procedure; variables with p >0.1 were not included in final models

[f] Model 2 considers maternal and infant prenatal variables, season starting growth interval and interactions and implements the full information maximum likelihood procedure; variables with p >0.1 were not included in final models

D.3 Association of fixed, time invariant[a] maternal and infant variables and maternal postpartum and infant postnatal[b] variables with weight velocity in the 1-4 month growth interval (g/month) using structural equation modeling[c] with and without the implementation of the full information maximum likelihood procedure

Variables	Model 1[d,e] (n=173)	Model 4[d,h] (n=332)
Female	-60.69 ± 11.69 p<0.001	-45.75 ± 9.34 p<0.001
Male	Ref	Ref
Newborn weight, g	54.13 ± 12.07 p<0.001	68.69 ± 11.929 p<0.001
Primiparous	15.51 ± 13.72 p=0.258	21.93 ± 12.59 p=0.081
Multiparous	Ref	Ref
Exclusively breastfed	20.04 ± 11.87 p=0.091	17.38 ± 9.89 p=0.079
Not exclusively breastfed	Ref	Ref
Received any vaccines	-33.27 ± 30.97 p=0.28	-20.35 ± 21.01 p=0.333
Received no vaccines	Ref	Ref
Child morbidity	-9.19 ± 4.20 p= 0.029	-6.32 ± 2.62 p=0.016
Higher agriculture tertile	-9.65 ± 12.88 p=0.454	-17.17 ± 10.68 p=0.108
Middle agriculture tertile	12.81 ± 17.39 p==0.46	11.45 ± 13.86 p=0.41
Lower agriculture tertile	Ref	Ref
Child morbidity*vaccination	8.28 ± 4.37 p= =0.058	5.01 ± 2.78 p=0.072
R^2	0.40	0.30

[a] Maternal and infant fixed prenatal variables include maternal height, parity, infant sex, gestational age and early neonatal length

[b] Maternal postpartum variables include morbidity, food security, diet diversity, weight velocity, and agricultural work; Infant postnatal variables include month starting the growth interval, morbidity, breastfeeding, vaccination and childcare

[c]All models control for village as a fixed effect

[d] Mean ± SE

[e] Model 1 considers maternal and infant prenatal variables, season starting growth interval and interactions and does not implement the full information maximum likelihood procedure; variables with p >0.1 were not included in final models

[f] Model 2 considers maternal and infant prenatal variables, season starting growth interval and interactions and implements the full information maximum likelihood procedure; variables with p >0.1 were not included in final models

REFERENCES

1. The World Health Organization: Physical Status: The Use and Interpretation of Anthropometry: Report of a WHO Expert Committee. Geneva 1995.
2. Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, Ezzati M, Grantham-McGregor S, Katz J, Martorell R, Uauy R: Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 2013, 382:427-451.
3. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, Sachdev HS: Maternal and child undernutrition: consequences for adult health and human capital. Lancet 2008, 371:340-357.
4. Schroeder DG, Martorell R, Rivera JA, Ruel MT, Habicht JP: Age differences in the impact of nutritional supplementation on growth. J Nutr 1995, 125:1051s-1059s.
5. Shrimpton R: Global policy and programme guidance on maternal nutrition: what exists, the mechanisms for providing it, and how to improve them? Paediatr Perinat Epidemiol 2012, 26 Suppl 1:315-325.
6. International Institute for Population Sciences: National Family health Survey-4. Mumbai, India. 2015-16.
7. International Institute for Population Sciences: National Family Health Survey-3. Mumbai, India.2005-06.
8. Garza C, de Onis M: Rationale for developing a new international growth reference. Food Nutr Bull 2004, 25:S5-14.
9. de Onis M, Onyango AW, Borghi E, Garza C, Yang H: Comparison of the World Health Organization Child Growth Standards and the National Center for Health Statistics/WHO international growth reference: implications for child health programmes. Public Health Nutr 2006, 9:942-947.
10. Victora CG, de Onis M, Hallal PC, Blossner M, Shrimpton R: Worldwide timing of growth faltering: revisiting implications for interventions. Pediatrics 2010, 125:e473-480.
11. Shrimpton R, Victora CG, de Onis M, Lima RA, Blössner M, Clugston G: Worldwide timing of growth faltering: implications for nutritional interventions. Pediatrics 2001, 107:e473-e480.
12. Patwari AK, Kumar S, Beard J: Undernutrition among infants less than 6 months of age: an underestimated public health problem in India. Matern Child Nutr 2015, 11:119-126.
13. Kerac M, Blencowe H, Grijalva-Eternod C, McGrath M, Shoham J, Cole TJ, Seal A: Prevalence of wasting among under 6-month-old infants in developing countries and implications of new case definitions using WHO growth standards: a secondary data analysis. Arch Dis Child 2011, 96:1008-1013.
14. Prost MA, Jahn A, Floyd S, Mvula H, Mwaiyeghele E, Mwinuka V, Mhango T, Crampin AC, McGrath N, Fine PE, Glynn JR: Implication of new WHO growth standards on identification of risk factors and estimated prevalence of malnutrition in rural Malawian infants. PLoS One 2008, 3:e2684.

15. Medhin G, Hanlon C, Dewey M, Alem A, Tesfaye F, Worku B, Tomlinson M, Prince M: Prevalence and predictors of undernutrition among infants aged six and twelve months in Butajira, Ethiopia: the P-MaMiE Birth Cohort. BMC Public Health 2010, 10:27.
16. Mason JB, Shrimpton R, Saldanha LS, Ramakrishnan U, Victora CG, Girard AW, McFarland DA, Martorell R: The first 500 days of life: policies to support maternal nutrition. Glob Health Action 2014, 7:23623.
17. Lee AC, Katz J, Blencowe H, Cousens S, Kozuki N, Vogel JP, Adair L, Baqui AH, Bhutta ZA, Caulfield LE, et al: National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle-income countries in 2010. Lancet Glob Health 2013, 1:e26-36.
18. Christian P, Lee SE, Donahue Angel M, Adair LS, Arifeen SE, Ashorn P, Barros FC, Fall CHD, Fawzi WW, Hao W, et al: Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. Int J Epidemiol 2013, 42:1340-1355.
19. Lee ACC, Kozuki N, Cousens S, Stevens GA, Blencowe H, Silveira MF, Sania A, Rosen HE, Schmiegelow C, Adair LS, et al: Estimates of burden and consequences of infants born small for gestational age in low and middle income countries with INTERGROWTH-21st standard: analysis of CHERG datasets. BMJ 2017, 358.
20. Katz J, Lee ACC, Kozuki N, Lawn JE, Cousens S, Blencowe H, Ezzati M, Bhutta ZA, Marchant T, Willey BA, et al: Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis. The Lancet 2013, 382:417-425.
21. Villar J, Smeriglio V, Martorell R, Brown CH, Klein RE: Heterogeneous growth and mental development of intrauterine growth-retarded infants during the first 3 years of life. Pediatrics 1984, 74:783-791.
22. Christian P, Lee SE, Donahue Angel M, Adair LS, Arifeen SE, Ashorn P, Barros FC, Fall CH, Fawzi WW, Hao W, et al: Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. Int J Epidemiol 2013, 42:1340-1355.
23. Khadilkar VV, Mandlik RM, Palande SA, Pandit DS, Chawla M, Nadar R, Chiplonkar SA, Kadam SS, Khadilkar AA: Growth status of small for gestational age Indian children from two socioeconomic strata. Indian J of Endocrinol and Metab 2016, 20:531-535.
24. UNICEF: Strategy for Improved Nutrition of Children and Women in Developing Countries. New York 1990.
25. Wu G, Bazer FW, Cudd TA, Meininger CJ, Spencer TE: Maternal Nutrition and Fetal Development. J Nutr 2004, 134:2169-2172.
26. Morrison JL, Regnault TRH: Nutrition in Pregnancy: Optimising Maternal Diet and Fetal Adaptations to Altered Nutrient Supply. Nutrients 2016, 8:342.
27. Dewey KG: Reducing stunting by improving maternal, infant and young child nutrition in regions such as South Asia: evidence, challenges and opportunities. Matern Child Nutr 2016, 12 Suppl 1:27-38.

28. Martorell R: Improved nutrition in the first 1000 days and adult human capital and health. Am J Hum Biol 2017, 29.
29. Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, Ezzati M, Grantham-McGregor S, Katz J, Martorell R, Uauy R: Maternal and child undernutrition and overweight in low-income and middle-income countries. The Lancet, 382:427-451.
30. Abu-Saad K, Fraser D: Maternal nutrition and birth outcomes. Epidemiol Rev 2010, 32:5-25.
31. Bhandari S, Sayami JT, Thapa P, Sayami M, Kandel BP, Banjara MR: Dietary intake patterns and nutritional status of women of reproductive age in Nepal: findings from a health survey. Arch Public Health 2016, 74:2.
32. Vir SC: Improving women's nutrition imperative for rapid reduction of childhood stunting in South Asia: coupling of nutrition specific interventions with nutrition sensitive measures essential. Matern Child Nutr 2016, 12:72-90.
33. Kramer MS, Kakuma R: Energy and protein intake in pregnancy. Cochrane Database Syst Rev 2003:Cd000032.
34. Imdad A, Bhutta ZA: Effect of balanced protein energy supplementation during pregnancy on birth outcomes. BMC Public Health 2011, 11 Suppl 3:S17.
35. Lechtig A, Habicht JP, Delgado H, Klein RE, Yarbrough C, Martorell R: Effect of food supplementation during pregnancy on birthweight. Pediatrics 1975, 56:508-520.
36. Panter-brick C: Motherhood and subsistence work: the Tamang of rural Nepal. Hum Ecol 1989, 17:205-228.
37. Singh J, Prentice AM, Diaz E, Coward WA, Ashford J, Sawyer M, Whitehead RG: Energy expenditure of Gambian women during peak agricultural activity measured by the doubly-labelled water method. Br J Nutr 1989, 62:315-329.
38. Dwarkanath P, Muthayya S, Vaz M, Thomas T, Mhaskar A, Mhaskar R, Thomas A, Bhat S, Kurpad A: The relationship between maternal physical activity during pregnancy and birth weight. Asia Pac J Clin Nutr 2007, 16:704-710.
39. Rao S, Kanade A, Margetts BM, Yajnik CS, Lubree H, Rege S, Desai B, Jackson A, Fall CHD: Maternal activity in relation to birth size in rural India. The Pune Maternal Nutrition Study. Eur J Clin Nutr 2009, 57:531-542.
40. Launer LJ: The work patterns of lactating women in Madura. Soc Sci Med 1993, 37:555-563.
41. Schlussel MM, Souza EB, Reichenheim ME, Kac G: Physical activity during pregnancy and maternal-child health outcomes: a systematic literature review. Cad Saude Publica 2008, 24 Suppl 4:s531-544.
42. Filippi V, Ronsmans C, Campbell OM, Graham WJ, Mills A, Borghi J, Koblinsky M, Osrin D: Maternal health in poor countries: the broader context and a call for action. Lancet 2006, 368:1535-1541.
43. Tanner JM: Catch-up growth in man. Br Med Bull 1981, 37:233-238.

44. Tudehope D, Vento M, Bhutta Z, Pachi P: Nutritional Requirements and Feeding Recommendations for Small for Gestational Age Infants. J Pediatr 2013, 162:S81-S89.
45. Rao S, Kanade AN, Yajnik CS, Fall CH: Seasonality in maternal intake and activity influence offspring's birth size among rural Indian mothers--Pune Maternal Nutrition Study. Int J Epidemiol 2009, 38:1094-1103.
46. Panter-Brick C: Seasonality of energy expenditure during pregnancy and lactation for rural Nepali women. Am J Clin Nutr 1993, 57:620-628.
47. Gillespie S, Harris J, Kadiyala S: The Agriculture-Nutrition Disconnect in India: What Do We Know? : International Food Policy Research Institute (IFPRI); 2012.
48. Prentice A, Prentice AM, Whitehead RG: Breast-milk fat concentrations of rural African women. 1. Short-term variations within individuals. Br J Nutr 1981, 45:483-494.
49. Brown KH, Akhtar NA, Robertson AD, Ahmed MG: Lactational capacity of marginally nourished mothers: relationships between maternal nutritional status and quantity and proximate composition of milk. Pediatrics 1986, 78:909-919.
50. Emmett PM, Rogers IS: Properties of human milk and their relationship with maternal nutrition. Early Hum Dev 1997, 49 Suppl:S7-28.
51. Prentice AM, Goldberg GR, Prentice A: Body mass index and lactation performance. Eur J Clin Nutr 1994, 48 Suppl 3:S78-86; discussion S86-79.
52. Stewart RC: Maternal depression and infant growth: a review of recent evidence. Matern Child Nutr 2007, 3:94-107.
53. Engle P, Menon P: Care and Nutrition: Concepts and Measurement. World Dev 1999, 27:1309-1337.
54. Barbosa L, Butte NF, Villalpando S, Wong WW, Smith EO: Maternal energy balance and lactation performance of Mesoamerindians as a function of body mass index. Am J Clin Nutr 1997, 66:575-583.
55. Bhutta ZA: Effect of infections and environmental factors on growth and nutritional status in developing countries. J Pediatr Gastroenterol Nutr 2006, 43 Suppl 3:S13-21.
56. Checkley W, Buckley G, Gilman RH, Assis AMO, Guerrant RL, Morris SS, Mølbak K, Valentiner-Branth P, Lanata CF, Black RE, et al: Multi-country analysis of the effects of diarrhoea on childhood stunting. Int J Epidemiol 2008, 37:816-830.
57. Martorell R, Habicht JP, Yarbrough C, Lechtig A, Klein RE, Western KA: Acute morbidity and physical growth in rural Guatemalan children. Am J Dis Child 1975, 129:1296-1301.
58. Adair LS, Guilkey DK: Age-specific determinants of stunting in Filipino children. J Nutr 1997, 127:314-320.
59. Prendergast A, Kelly P: Enteropathies in the developing world: neglected effects on global health. Am J Trop Med Hyg 2012, 86:756-763.

60. Paul VK, Sachdev HS, Mavalankar D, Ramachandran P, Sankar MJ, Bhandari N, Sreenivas V, Sundararaman T, Govil D, Osrin D, Kirkwood B: Reproductive health, and child health and nutrition in India: meeting the challenge. Lancet 2011, 377:332-349.
61. Shaikh BT, Hatcher J: Health seeking behaviour and health service utilization in Pakistan: challenging the policy makers. J Public Health (Oxf) 2005, 27:49-54.
62. Kumar S: India health survey finds too many women and children in poor health. The Lancet 2000, 356:1830.
63. Balarajan Y, Selvaraj S, Subramanian SV: Health care and equity in India. Lancet 2011, 377:505-515.
64. Jones AD, Rukobo S, Chasekwa B, Mutasa K, Ntozini R, Mbuya MNN, Stoltzfus RJ, Humphrey JH, Prendergast AJ: Acute Illness Is Associated with Suppression of the Growth Hormone Axis in Zimbabwean Infants. Am J Trop Med Hyg 2015, 92:463-470.
65. Arifeen S, Black RE, Antelman G, Baqui A, Caulfield L, Becker S: Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. Pediatrics 2001, 108:E67.
66. Victora CG, Bahl R, Barros AJD, França GVA, Horton S, Krasevec J, Murch S, Sankar MJ, Walker N, Rollins NC: Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. The Lancet 2016, 387:475-490.
67. Rasheed S, Frongillo EA, Devine CM, Alam DS, Rasmussen KM: Maternal, infant, and household factors are associated with breast-feeding trajectories during infants' first 6 months of life in Matlab, Bangladesh. J Nutr 2009, 139:1582-1587.
68. Marriott BP, White A, Hadden L, Davies JC, Wallingford JC: World Health Organization (WHO) infant and young child feeding indicators: associations with growth measures in 14 low-income countries. Matern Child Nutr 2012, 8:354-370.
69. Stuebe A: The Risks of Not Breastfeeding for Mothers and Infants. Rev Obstet Gynecol 2009, 2:222-231.
70. Kadiyala S, Harris J, Headey D, Yosef S, Gillespie S: Agriculture and nutrition in India: mapping evidence to pathways. Ann NY Acad Sci 2014, 1331:43-56.
71. Headey D, Chiu A, Kadiyala S: Agriculture's role in the Indian enigma: help or hindrance to the crisis of undernutrition? Food Secur 2012, 4:87-102.
72. Devereux S, Sabates-Wheeler R, Longhurst R: Seasonality, Rural Livelihoods and Development. New York, NY; London: Earthscan; 2012.
73. Prentice AM, Cole TJ: Seasonal changes in growth and energy status in the Third World. Proc Nutr Soc 1994, 53:509-519.
74. Ulijaszek S S, SS. (Ed.). Seasonality and Human Ecolog. Cambridge, UK: Cambridge University Press; 1993.

75. Chambers R: Seasonal Poverty: Integrated, overlooked and therefore opportunity. In Seasonality, Rural LIvelihoods and Development. Edited by Devereux S, Sabates-Wheeler R, Longhurst R. London and New York: Earthscan; 2012: 76-92
76. Prendergast AJ, Humphrey JH: The stunting syndrome in developing countries. Paediatr Int Child Health 2014, 34:250-265.
77. Humphrey JH: Child undernutrition, tropical enteropathy, toilets, and handwashing. Lancet 2009, 374:1032-1035.
78. Hoppe C, Molgaard C, Michaelsen KF: Cow's milk and linear growth in industrialized and developing countries. Annu Rev Nutr 2006, 26:131-173.
79. Clemmons DR: The relative roles of growth hormone and IGF-1 in controlling insulin sensitivity. J Clin Invest 2004, 113:25-27.
80. Fazeli PK, Klibanski A: Determinants of Growth Hormone Resistance in Malnutrition. J Endocrinol 2014, 220:R57-R65.
81. Shils M SM, Ross AC, Caballero B, Cousins RJ.: Modern Nutrition in Health and Disease. 10th ed edn. Philadelphia: Lippincott Williams and Wilkins; 2006.
82. Soliman AT, ElZalabany MM, Salama M, Ansari BM: Serum leptin concentrations during severe protein-energy malnutrition: correlation with growth parameters and endocrine function. Metabolism 2000, 49:819-825.
83. Soliman AT, Yasin M, Kassem A: Leptin in pediatrics: A hormone from adipocyte that wheels several functions in children. Indian J Endocr Metab 2012, 16:S577-S587.
84. Dewey KG, Hawck MG, Brown KH, Lartey A, Cohen RJ, Peerson JM: Infant weight-for-length is positively associated with subsequent linear growth across four different populations. Matern Child Nutr 2005, 1:11-20.
85. Richard SA, Black RE, Checkley W: Revisiting the Relationship of Weight and Height in Early Childhood. Adv Nutr 2012, 3:250-254.
86. Richard SA, Black RE, Gilman RH, Guerrant RL, Kang G, Lanata CF, Molbak K, Rasmussen ZA, Sack RB, Valentiner-Branth P, Checkley W: Catch-up growth occurs after diarrhea in early childhood. J Nutr 2014, 144:965-971.
87. Le Mare L, Audet K: A longitudinal study of the physical growth and health of postinstitutionalized Romanian adoptees. J Paediatr Child Health 2006, 11:85-91.
88. Outes I, Porter C: Catching up from early nutritional deficits? Evidence from rural Ethiopia. Econ Hum Biol 2013, 11:148-163.
89. Schott WB, Crookston BT, Lundeen EA, Stein AD, Behrman JR: Periods of child growth up to age 8 years in Ethiopia, India, Peru and Vietnam: Key distal household and community factors. Soc Sci Med 2013, 97:278-287.
90. Chodick G, Flash S, Deoitch Y, Shalev V: Seasonality in birth weight: review of global patterns and potential causes. Hum Biol 2009, 81:463-477.
91. Shaheen R, de Francisco A, El Arifeen S, Ekstrom EC, Persson LA: Effect of prenatal food supplementation on birth weight: an observational study from Bangladesh. Am J Clin Nutr 2006, 83:1355-1361.

92. Roberts SB, Paul AA, Cole TJ, Whitehead RG: Seasonal changes in activity, birth weight and lactational performance in rural Gambian women. Trans R Soc Trop Med Hyg 1982, 76:668-678.
93. Rashid H, Kagami M, Ferdous F, Ma E, Terao T, Hayashi T, Wagatsuma Y: Temperature during pregnancy influences the fetal growth and birth size. Trop Med Health 2017, 45:1.
94. Neufeld L, Pelletier DL, Haas JD: The timing hypothesis and body proportionality of the intra-uterine growth retarded infant. Am J Hum Biol 1999, 11:638-646.
95. Rayco-Solon P, Fulford AJ, Prentice AM: Differential effects of seasonality on preterm birth and intrauterine growth restriction in rural Africans. Am J Clin Nutr 2005, 81:134-139.
96. Brown KH, Black RE, Becker S: Seasonal changes in nutritional status and the prevalence of malnutrition in a longitudinal study of young children in rural Bangladesh. Am J Clin Nutr 1982, 36:303-313.
97. Pollitt E, Arthur J: Seasonality and weight gain during the first year of life. Am J Hum Biol 1989, 1:747-756.
98. Maleta K, Virtanen S, Espo M, Kulmala T, Ashorn P: Timing of growth faltering in rural Malawi. Arch Dis Child 2003, 88.
99. Brown KH, Black RE, Robertson AD, Becker S: Effects of season and illness on the dietary intake of weanlings during longitudinal studies in rural Bangladesh. Am J Clin Nutr 1985, 41:343-355.
100. Das A, Chatterjee R, Karthick M, Mahapatra T, Chaudhuri I: The Influence of Seasonality and Community-Based Health Worker Provided Counselling on Exclusive Breastfeeding - Findings from a Cross-Sectional Survey in India. PLoS One 2016, 11:e0161186.
101. Panter-Brick C: Lactation, birth spacing and maternal work-loads among two castes in rural Nepal. J Biosoc Sci 1991, 23:137-154.
102. Jagai JS, Sarkar R, Castronovo D, Kattula D, McEntee J, Ward H, Kang G, Naumova EN: Seasonality of rotavirus in South Asia: a meta-analysis approach assessing associations with temperature, precipitation, and vegetation index. PLoS One 2012, 7:e38168.
103. Rousham EK, Mascie-Taylor CGN: Seasonality and child morbidity in rural Bangladesh. Am J Hum Biol 1995, 7:369-379.
104. Chambers R, Longhurst R, Bradley D, Feachem R: Seasonal dimensions to rural porverty: analysis and practical implications. J Trop Med Hyg 1979, 82:156-172.
105. Zeitlin MF, Ahmed NU, Beiser AS, Zeitlin JA, Super CM, Guldan GS: Developmental, behavioural, and environmental risk factors for diarrhoea among rural Bangladeshi children of less than two years. J Diarrhoeal Dis Res 1995, 13:99-105.
106. Pathela P, Zahid Hasan K, Roy E, Huq F, Kasem Siddique A, Bradley Sack R: Diarrheal illness in a cohort of children 0-2 years of age in rural Bangladesh: I. Incidence and risk factors. Acta Paediatr 2006, 95:430-437.

107. Bang AT, Reddy HM, Baitule SB, Deshmukh MD, Bang RA: The incidence of morbidities in a cohort of neonates in rural Gadchiroli, India: seasonal and temporal variation and a hypothesis about prevention. J Perinatol 2005, 25 Suppl 1:S18-28.
108. Rupa V, Isaac R, Manoharan A, Jalagandeeswaran R, Thenmozhi M: Risk factors for upper respiratory infection in the first year of life in a birth cohort. Int J Pediatr Otorhinolaryngol 2012, 76:1835-1839.
109. Stevens B, Watt K, Brimbecombe J, Clough A, Judd J, Lindsay D: The role of seasonality on the diet and household food security of pregnant women living in rural Bangladesh: a cross-sectional study. Public Health Nutr 2017, 20:121-129.
110. Schmid MA, Salomeyesudas B, Satheesh P, Hanley J, Kuhnlein HV: Intervention with traditional food as a major source of energy, protein, iron, vitamin C and vitamin A for rural Dalit mothers and young children in Andhra Pradesh, South India. Asia Pac J Clin Nutr 2007, 16:84-93.
111. Haas JD, Brownlie Tt: Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship. J Nutr 2001, 131:676S-688S; discussion 688S-690S.
112. A F-L, F B: Nutritional seasonality: The dimension of the problem. In: Uliaszek SJ (ed.) Seasonality and Human Ecology. In Seasonality and Human Ecology. 1993: pp.147–165.
113. Chambers R: Seasonal poverty: integrated, overlooked and therfore opportunity. In Seasonality, Rural Livelihoods and Development Edited by Devereux S, Sabates-Wheeler R, Longhurst R. New York, NY; London: Earthscan; 2012: 76-92
114. Easterling DR, Meehl GA, Parmesan C, Changnon SA, Karl TR, Mearns LO: Climate extremes: observations, modeling, and impacts. Science 2000, 289:2068-2074.
115. Maps of India [https://www.mapsofindia.com]
116. International Institute for Population Sciences: National Family Health Survey-4 (NFHS-4) State Fact Sheet :Uttar Pradesh. Mumbai, India. 2015-2016.
117. Climate: Rae Bareli [https://en.climate-data.org/location/24659/]
118. Villar J, Giuliani F, Bhutta ZA, Bertino E, Ohuma EO, Ismail LC, Barros FC, Altman DG, Victora C, Noble JA, et al: Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21st Project. Lancet Glob Health 2016, 3:e681-e691.
119. Lohman TG, Roche AF, Martorell R: Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books; 1988.
120. de Onis M, Onyango AW, Van den Broeck J, Chumlea WC, Martorell R: Measurement and standardization protocols for anthropometry used in the construction of a new international growth reference. Food Nutr Bull 2004, 25:S27-36.

121. Li F, Wilkens LR, Novotny R, Fialkowski MK, Paulino YC, Nelson R, Bersamin A, Martin U, Deenik J, Boushey CJ: Anthropometric Measurement Standardization in the US-Affiliated Pacific: Report from the Children's Healthy Living Program. Am J Hum Biol 2016, 28:364-371.
122. Villar J, Cheikh Ismail L, Victora CG, Ohuma EO, Bertino E, Altman DG, Lambert A, Papageorghiou AT, Carvalho M, Jaffer YA, et al: International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet 2014, 384:857-868.
123. StataCorp: Stata Statistical Software: Release 13. College Station, TX: StataCorp LP; 2013.
124. World Health Organization: WHO Anthro 2005 for personal computers manual: software for assessing growth and development of the world's children. Geneva: World Health Organization 2006.
125. Lokshin M, Radyakin S: Month of Birth and Children's Health in India. J Hum Resour 2012, 47:174-203.
126. Adair LS: Low Birth Weight and Intrauterine Growth Retardation in Filipino Infants. Pediatrics 1989, 84:613-622.
127. Arifeen SE, Black RE, Caulfield LE, Antelman G, Baqui AH: Determinants of infant growth in the slums of Dhaka: size and maturity at birth, breastfeeding and morbidity. Eur J Clin Nutr 2001, 55:167-178.
128. Katz J, Wu LA, Mullany LC, Coles CL, Lee ACC, Kozuki N, Tielsch JM: Prevalence of Small-for-Gestational-Age and Its Mortality Risk Varies by Choice of Birth-Weight-for-Gestation Reference Population. PLoS ONE 2014, 9:e92074.
129. Lima M, Ismail S, Ashworth A, Morris SS: Influence of heavy agricultural work during pregnancy on birthweight in northeast Brazil. Int J Epidemiol 1999, 28:469-474.
130. Blumenshine P, Egerter S, Barclay CJ, Cubbin C, Braveman PA: Socioeconomic Disparities in Adverse Birth Outcomes. Am J Prev Med 39:263-272.
131. Metgud CS, Naik VA, Mallapur MD: Factors affecting birth weight of a newborn--a community based study in rural Karnataka, India. PLoS One 2012, 7:e40040.
132. Kozuki N, Lee AC, Silveira MF, Sania A, Vogel JP, Adair L, Barros F, Caulfield LE, Christian P, Fawzi W, et al: The associations of parity and maternal age with small-for-gestational-age, preterm, and neonatal and infant mortality: a meta-analysis. BMC Public Health 2013, 13:S2.
133. Government of Uttar Pradesh: Uttar Pradesh District Census Handbook. Uttar Pradesh, India: Census of India; 2011.
134. Carlson RV, Boyd KM, Webb DJ: The revision of the Declaration of Helsinki: past, present and future. Br J Clin Pharmacol 2004, 57:695-713.
135. World Health Organization (WHO): WHO Anthro 2005 for personal computers manual: software for assessing growth and development of the world's children. Geneva: World Health Organization 2006.

136. Oluwafemi OR, Njokanma FO, Disu EA, Ogunlesi TA: Current pattern of Ponderal Indices of term small-for-gestational age in a population of Nigerian babies. BMC Pediatrics 2013, 13:110.
137. Coates J, Swindale, A, Bilinksy, P.: Household Food Insecurity Access Scale (HFIAS) for Measurement of Household Food Access: Indicator Guide (v. 3). Academy for Educational Development 2007, 3.
138. Vyas S, Kumaranayake, L.: Constructing socio-economic status indices: how to use principal components analysis. Health Policy Plan 2006, 21:459-468.
139. Dong Y, Peng C-YJ: Principled missing data methods for researchers. SpringerPlus 2013, 2:222.
140. Lampl M, Jeanty P: Timing is everything: a reconsideration of fetal growth velocity patterns identifies the importance of individual and sex differences. Am J Hum Biol 2003, 15:667-680.
141. Roland MCP, Friis CM, Voldner N, Godang K, Bollerslev J, Haugen G, Henriksen T: Fetal Growth versus Birthweight: The Role of Placenta versus Other Determinants. PLoS ONE 2012, 7:e39324.
142. Holroyd CR, Harvey NC, Crozier SR, Winder NR, Mahon PA, Ntami G, Godfrey KM, Inskip HM, Cooper C, the SWSSG: Placental size at 19 weeks predicts offspring bone mass at birth: Findings from the Southampton Women's Survey. Placenta 2012, 33:623-629.
143. Murray LJ, O'Reilly DP, Betts N, Patterson CC, Davey Smith G, Evans AE: Season and outdoor ambient temperature: effects on birth weight. Obstet Gynecol 2000, 96:689-695.
144. Hinkle SN, Albert PS, Mendola P, Sjaarda LA, Yeung E, Boghossian NS, Laughon SK: The association between parity and birthweight in a longitudinal consecutive pregnancy cohort. Paediatr Perinat Epidemiol 2014, 28:106-115.
145. Borders AE, Grobman WA, Amsden LB, Holl JL: Chronic stress and low birth weight neonates in a low-income population of women. Obstet Gynecol 2007, 109:331-338.
146. Agarwal N, Aiyar A, Bhattacharjee A, Cummins J, Gunadi C, Singhania D, Taylor M, Wigton-Jones E: Month of birth and child height in 40 countries. Econ Lett 2017, 157:10-13.
147. Noel-Weiss J, Courant G, Woodend AK: Physiological weight loss in the breastfed neonate: a systematic review. Open Med 2008, 2:e99-e110.
148. Thulier D: Weighing the Facts: A Systematic Review of Expected Patterns of Weight Loss in Full-Term, Breastfed Infants. J Hum Lact 2015, 32.
149. Black RE, Brown KH, Becker S, Alim AR, Huq I: Longitudinal studies of infectious diseases and physical growth of children in rural Bangladesh. II. Incidence of diarrhea and association with known pathogens. Am J Epidemiol 1982, 115.
150. Panter-Brick C: Seasonal growth patterns in rural Nepali children. Ann Hum Biol 1997, 24:1-18.
151. Costello AM: Growth velocity and stunting in rural Nepal. Arch Dis Child 1989, 64:1478-1482.

152. Xu X, Wang WP, Guo ZP, Cheung YB, Karlberg J: Seasonality of growth in Shanghai infants (n=4128) born in 11 consecutive years. Eur J Clin Nutr 2001, 55:714-725.
153. Rabe-Hesketh S, & Skrondal, A.: Multilevel and longitudinal modeling using Stata. College Station, TX: Stata Press.; 2008.
154. Saha KK, Frongillo EA, Alam DS, Arifeen SE, Persson LA, Rasmussen KM: Household food security is associated with growth of infants and young children in rural Bangladesh. Public Health Nutr 2009, 12:1556-1562.
155. Dewey KG, Huffman SL: Maternal, infant, and young child nutrition: combining efforts to maximize impacts on child growth and micronutrient status. Food Nutr Bull 2009, 30:S187-189.
156. de Onis M, Branca F: Childhood stunting: a global perspective. Matern Child Nutr 2016, 12 Suppl 1:12-26.
157. de Onis and the WHO Multicentre Growth References Study Group: WHO Child Growth Standards Growth velocity based on weight, length and head circumference: Methods and development. Geneva: World Health Organization (WHO); 2009.
158. Gillespie S, McNeill G: Food, Health and Survival in India and Developing Countries. New Delhi, India: Oxford India Paperbacks; 1994.
159. Maleta K, Virtanen SM, Espo M, Kulmala T, Ashorn P: Seasonality of growth and the relationship between weight and height gain in children under three years of age in rural Malawi. Acta Paediatr 2003, 92:491-497.
160. Rosenfeld RG: Insulin-like growth factors and the basis of growth. N Engl J Med 2003, 349:2184-2186.
161. Lampl M: Human growth from the cell to the organism: saltations and integrative physiology. Ann Hum Biol 2009, 36:478-495.
162. Iannotti LL, Zavaleta N, Huasaquiche C, Leon Z, Caulfield LE: Early growth velocities and weight gain plasticity improve linear growth in Peruvian infants. Matern Child Nutr 2015, 11:127-137.
163. Maleta K, Virtanen SM, Espo M, Kulmala T, Ashorn P: Childhood malnutrition and its predictors in rural Malawi. Paediatr Perinat Epidemiol 2003, 17:384-390.
164. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, Sachdev HS, for the Maternal Child Undernutrition Study Group: Maternal and child undernutrition: consequences for adult health and human capital. Lancet 2008, 371:340-357.
165. World Health Organization: Indicators for assessing infant and young child feeding practices. Part I: definition. Geneva 2008.
166. Sabina Alkire HM, Ruth Meinzen-Dick, Amber Peterman, Agnes Quisumbing, Greg Seymour, and Ana Vaz: Instructional Guide on the Women's Empowerment in Agriculture Index. World Dev 2013, 52:71-91.
167. FANTA: Minimum Dietary Diversity for Women: A guide to measurement. Rome: FAO; 2016.
168. VanderWeele TJ: Mediation Analysis: A Practitioner's Guide. Annu Rev Public Health 2016, 37:17-32.

169. Dewey KG, Mayers DR: Early child growth: how do nutrition and infection interact? Matern Child Nutr 2011, 7 Suppl 3:129-142.
170. Bohler E, Aalen O, Bergstrom S, Halvorsen S: Breast feeding and seasonal determinants of child growth in weight in east Bhutan. Acta Paediatr 1995, 84:1029-1034.
171. Sinha B, Taneja S, Chowdhury R, Mazumder S, Rongsen-Chandola T, Upadhyay RP, Martines J, Bhandari N, Bhan MK: Low-birthweight infants born to short-stature mothers are at additional risk of stunting and poor growth velocity: Evidence from secondary data analyses. Matern Child Nutr 2018, 14.
172. Delgado HL, Valverde VE, Martorell R, Klein RE: Relationship of maternal and infant nutrition to infant growth. Early Hum Dev 1982, 6:273-286.
173. Hindmarsh PC, Geary MPP, Rodeck CH, Kingdom JCP, Cole TJ: Factors Predicting Ante- and Postnatal Growth. Pediatr Res 2008, 63:99.
174. Haas JD, Balcazar H, Caulfield L: Variation in early neonatal mortality for different types of fetal growth retardation. Am J Phys Anthropol 1987, 73:467-473.
175. Caulfield LE, Haas JD, Belizan JM, Rasmussen KM, Edmonston B: Differences in early postnatal morbidity risk by pattern of fetal growth in Argentina. Paediatr Perinat Epidemiol 1991, 5:263-275.
176. Dewey KG, Cohen RJ, Brown KH, Rivera LL: Effects of exclusive breastfeeding for four versus six months on maternal nutritional status and infant motor development: results of two randomized trials in Honduras. J Nutr 2001, 131:262-267.
177. Lamberti LM, Zakarija-Grković I, Fischer Walker CL, Theodoratou E, Nair H, Campbell H, Black RE: Breastfeeding for reducing the risk of pneumonia morbidity and mortality in children under two: a systematic literature review and meta-analysis. BMC Public Health 2013, 13:S18-S18.
178. Biering-Sørensen S, Andersen A, Ravn H, Monterio I, Aaby P, Benn CS: Early BCG vaccine to low-birth-weight infants and the effects on growth in the first year of life: a randomised controlled trial. BMC Pediatrics 2015, 15:137.
179. Shin T, Davison ML, Long JD: Maximum likelihood versus multiple imputation for missing data in small longitudinal samples with nonnormality. Psychol Methods 2017, 22:426-449.
180. Mamidi RS, Shidhaye P, Radhakrishna KV, Babu JJ, Reddy PS: Pattern of growth faltering and recovery in under 5 children in India using WHO growth standards--a study on First and Third National Family Health Survey. Indian Pediatr 2011, 48:855-860.
181. Saha KK, Frongillo EA, Alam DS, Arifeen SE, Persson LA, Rasmussen KM: Appropriate infant feeding practices result in better growth of infants and young children in rural Bangladesh. Am J Clin Nutr 2008, 87:1852-1859.
182. Sanghvi U, Thankappan KR, Sarma PS, Sali N: Assessing potential risk factors for child malnutrition in rural Kerala, India. J Trop Pediatr 2001, 47:350-355.
183. Moore SR, Lima AA, Conaway MR, Schorling JB, Soares AM, Guerrant RL: Early childhood diarrhoea and helminthiases associate with long-term linear growth faltering. Int J Epidemiol 2001, 30:1457-1464.

184. Lakshminarayanan S, Jayalakshmy R: Diarrheal diseases among children in India: Current scenario and future perspectives. J Nat Sc Biol Med 2015, 6:24-28.
185. Fischer Walker CL, Aryee MJ, Boschi-Pinto C, Black RE: Estimating Diarrhea Mortality among Young Children in Low and Middle Income Countries. PLoS ONE 2012, 7:e29151.
186. Checkley W, Epstein LD, Gilman RH, Cabrera L, Black RE: Effects of acute diarrhea on linear growth in Peruvian children. Am J Epidemiol 2003, 157:166-175.
187. Assis AM, Barreto ML, Santos LM, Fiaccone R, da Silva Gomes GS: Growth faltering in childhood related to diarrhea: a longitudinal community based study. Eur J Clin Nutr 2005, 59:1317-1323.
188. Rowland MG, Rowland SG, Cole TJ: Impact of infection on the growth of children from 0 to 2 years in an urban West African community. Am J Clin Nutr 1988, 47:134-138.
189. Kossmann J, Nestel P, Herrera MG, El-Amin A, Fawzi WW: Undernutrition and childhood infections: a prospective study of childhood infections in relation to growth in the Sudan. Acta Paediatr 2000, 89:1122-1128.
190. Smith TA, Lehmann D, Coakley C, Spooner V, Alpers MP: Relationships between growth and acute lower-respiratory infections in children aged less than 5 y in a highland population of Papua New Guinea. Am J Clin Nutr 1991, 53:963-970.
191. Frith AL, Naved RT, Ekström E-C, Rasmussen KM, Frongillo EA: Micronutrient supplementation affects maternal-infant feeding interactions and maternal distress in Bangladesh. Am J Clin Nutr 2009, 90:141-148.
192. Rahmanifar A, Kirksey A, Wachs TD, McCabe GP, Bishry Z, Galal OM, Harrison GG, Jerome NW: Diet during lactation associated with infant behavior and caregiver-infant interaction in a semirural Egyptian village. J Nutr 1993, 123:164-175.
193. Mwase I, Mutoro A, Owino V, Garcia AL, Wright CM: Poor Infant Feeding Practices and High Prevalence of Malnutrition in Urban Slum Child Care Centres in Nairobi: A Pilot Study. J Trop Pediatr 2016, 62:46-54.
194. Patel V, Rahman A, Jacob KS, Hughes M: Effect of maternal mental health on infant growth in low income countries: new evidence from South Asia. BMJ 2004, 328:820-823.
195. Kulwa KB, Kinabo JL, Modest B: Constraints on good child-care practices and nutritional status in urban Dar-es-Salaam, Tanzania. Food Nutr Bull 2006, 27:236-244.
196. Chaturvedi S, Ramji S, Arora NK, Rewal S, Dasgupta R, Deshmukh V: Time-constrained mother and expanding market: emerging model of under-nutrition in India. BMC Public Health 2016, 16:632.
197. Rasmussen KM: The Influence of Maternal Nutrition on Lactation. Annu Rev Nutr 1992, 12:103-117.
198. Currie J, Vogl T: Early-Life Health and Adult Circumstance in Developing Countries. Annu Rev Econom 2013, 5:1-36.

199. Moore SE: Early life nutritional programming of health and disease in The Gambia. J Dev Orig Health Dis 2016, 7:123-131.
200. Vaiserman AM: Epigenetic programming by early-life stress: Evidence from human populations. Dev Dyn 2015, 244:254-265.
201. Sabates-Wheeler R, Devereux S: From seasonal lives towards a-seasonal living: builidng seasonality into risk managment response In Seasonality, Rural Livelihoods and Development Edited by Devereux S, Sabates-Wheeler R, Longhurst R. New York, NY; London: Earthscan; 2012: 278-295
202. Publications & Tools: Dataset [https://www.ifpri.org/publications?=&f%5B0%5D=sm_content_subtype_to_terms%3D1&f%5B1%5D=sm_content_subtype_to_terms%3A5605]
203. International Food Policy Research I, Data A, Technical Assistance L: Bangladesh Alive & Thrive Baseline Survey 2010. Harvard Dataverse; 2017.
204. Living Standards Measurement Study (LSMS) [http://surveys.worldbank.org/lsms]
205. Cunningham K, Singh A, Pandey Rana P, Brye L, Alayon S, Lapping K, Gautam B, Underwood C, Klemm RDW: Suaahara in Nepal: An at-scale, multi-sectoral nutrition program influences knowledge and practices while enhancing equity. Matern Child Nutr 2017, 13.
206. Beusenberg M OJ: A User's guide to the self reporting questionnaire (SRQ). Geneva: World Health Organization.; 1994.
207. van der Westhuizen C, Wyatt G, Williams JK, Stein DJ, Sorsdahl K: Validation of the Self Reporting Questionnaire 20-Item (SRQ-20) for Use in a Low- and Middle-Income Country Emergency Centre Setting. Int J Ment Health Addict 2016, 14:37-48.
208. Swindale A, Bilinsky P: Development of a universally applicable household food insecurity measurement tool: process, current status, and outstanding issues. J Nutr 2006, 136:1449s-1452s.
209. Coates J, Frongillo EA, Rogers BL, Webb P, Wilde PE, Houser R: Commonalities in the experience of household food insecurity across cultures: what are measures missing? J Nutr 2006, 136:1438s-1448s.
210. Martin-Prevel Y AP, Wiesmann D Moving Forward on Choosing a Standard Operational Indicator of Women's Dietary Diversity. Rome: FAO; 2015.
211. Working Group on Infant and Young Child Feeding Indicators: eveloping and Validating Simple Indicators of Dietary Quality and Energy Intake of Infants and Young Children in Developing Countries: Summary of Findings from Analysis of 10 Data Sets. Washington, DC: Food and Nutrition Technical Assistance Project/Academy for Educational Development; 2006.
212. Alkire S, Meinzen-Dick R, Peterman A, Quisumbing AR, Seymour G, A V: The Women's Empowerment in Agriculture Index. In IFPRI Discussion Paper. Washington, DC: IFPRI; 2012.
213. World Health Organization: Indicators for Assessing Infant and Young Child Feeding Practices. Part 2. Measurements. Geneva 2008.